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THE MONTH

DIETETICS and nutrition have long been the happy hunting ground of the faddists—both within and without the profession. Even the nutritionists have tended to go off the rails with disturbing frequency in their pronouncements on the relevance of experimental animal work to the health and well-being of mankind. The result is that the clinician finds it increasingly difficult to know where to turn for advice and help. It is with a view to clarifying the more controversial aspects of the subject that we have planned the symposium on 'Diet and Nutrition' this month. The opening two articles—on 'The problem of obesity' and 'Fatty acids and coronary disease'—deal with the most controversial of all these problems, but only slightly less controversial are the subjects of the last two articles—'Nutrition and athletics' and 'Diet and allergy'. 'Nutrition and infection' is a subject on which many dogmatic statements are made but Dr. Cuthbertson's authoritative review of this important problem amply confirms his conclusion that 'the ability to confer or alter resistance to infection through dietary means is a property much more complex than is usually considered by nutritionists'. Equally typical of our lack of fundamental knowledge is the fact that Professor Tunbridge finds that he can best sum up our present knowledge of 'Nutrition and old age' by a quotation from 1596. The remaining article in the symposium, on 'Malnutrition in the Tropics', will provide our many readers in Africa and Asia with an admirably practical and authoritative review of this, perhaps the most pressing, medical problem in the world at the present moment.

The Symposium

'THE more the hospital services are studied, the greater is the revelation of the complementary role of the other medical and ancillary services'. Such is one of the many trenchant comments in the introduction to the twenty-first anniversary issue of the report of the Nuffield Provincial Hospitals Trust. This, the fifth report of the Trust, covers the period 1958-61, and provides ample evidence of the admirable work the Trust is doing in the field of integration of the varying aspects of the National Health Service. The schemes which the Trust has sponsored, and upon which it has spent over £1 million in the period under review, 'cover', as the report points out, 'most of the many facets of the health services'.

The G.P. in Focus

Eight of these schemes are concerned with general practice, and two of them are of particular interest in so far as they stress the social background

to the general practitioner's work. In other words they emphasize the role of the general practitioner as the family doctor and not merely the purveyor of pills or the conveyor belt to hospital. In one of these schemes a grant from the Trust has allowed a social worker to be seconded to a group practice in Rugeley. In this practice of nearly 12,000 patients, the social worker has made over 1,700 home visits and had 2,500 interviews at the surgery in a period of two years. In the words of the report, she 'has linked up with the local social services to bring practical help and advice to families faced with financial, housing and unemployment difficulties and the worries of looking after aged and sick relatives', and, in the opinion of the general practitioners concerned, 'she has now become invaluable'. In the other scheme, in Cardiff, the deputy head almoner of the United Cardiff Hospitals has been seconded to a four-doctor practice. In addition to seeing patients recognized by the partners as having a social problem needing casework help, she is also 'doing a number of routine investigations in an attempt to identify at what point in illness social problems are most likely to arise'.

Fire-proof Clothing

For over three hundred years attempts have been made to produce non-inflammable textiles, and the first relevant patent was taken out in this country in 1735. Yet we still hear much about the dangers of flammable clothing. The problem, however, is not as simple as some would make it out to be. Apart from anything else, as F. Ward (*J. Roy. Inst. publ. Hlth*, 1961, **24**, 55) pointed out in a recent lecture, the non-inflammable textiles available are not being taken up by the public. Polyvinyl chloride, for instance, is virtually non-inflammable and nylon, though it can be made to burn in certain circumstances, is difficult to ignite. Cotton, viscose rayon and wool, on the other hand, are all flammable. Yet, in spite of this, the newer fibres such as nylon occupy only 4 per cent. of the market, whilst cotton occupies 42 to 45 per cent., viscose rayon 42 to 45 per cent., and wool 27 to 32 per cent.

Although flame-proofing is perfectly feasible, there are certain practical difficulties. Thus, treating a fabric with a solution of borax and boric acid will prevent its bursting into flame although it will char as long as it is in contact with the source of heat. Unfortunately the proofing salts are removed when the fabric is washed. Progress is being made, however, and there are now treatments available on cellulosic fabrics which are suitable for certain purposes. Meanwhile much could be done by what Ward nicely describes as 'intelligent living'. As he notes, 'many accidents have occurred to young and old people wearing flowing nightdresses which would not have occurred if they had been clothed in pyjamas'. Is there any reason why the traditional nightgown for these two sections of the community should not be modernized? Equally relevant is his reminder that, 'if all open fires were adequately guarded, there would be little opportunity for clothes to become ignited'.

Is Toxæmia of Pregnancy Psychosomatic?

As C. A. Douglas Ringrose (*Canad. med. Ass. J.*, 1961, **84**, 647) points out, 'no organic theory for the etiology of toxæmia appears to have universal support'. He therefore comes forward with the interesting if provocative suggestion that it may be 'a psychosomatic disorder'. This is by no means a novel suggestion. Ringrose himself quotes an 1812 writer as saying: 'Have indulgence for the pregnant woman's complaints, listen to her desires with complaisance, console her, and in place of the severity of the doctor adopt rather the affectionate tone of her friend or her father'. He also notes the much more recent case of the Mexican girl seized by the police and placed in jail on suspicion of a felony. A few hours earlier an antenatal examination had revealed no abnormality. The morning after being arrested she was in the throes of eclamptic convulsions.

In an attempt to clarify the issue, Ringrose reports the results of Minnesota Multiphasic Personality Inventory (M.M.P.I.) tests in a group of 41 pregnant unmarried mothers during the last half of their pregnancies. Eight of them developed pre-eclampsia and 14 had 'incipient pre-eclampsia'. As judged by the test, nine of the 14 patients (64 per cent.) with incipient pre-eclampsia and six of the eight (75 per cent.) with pre-eclampsia had abnormal personalities, compared with only six of the 19 (32 per cent.) who did not develop pre-eclampsia. 'Statistical analysis of the correlation between emotional instability and toxæmia', it is stated, 'reveals that there is only one possibility in 20 that these results could occur by chance alone'. On the other hand, 'the type of personality deviation was not constant'. These results are clearly no more than a possible clue to the etiology of this disturbing condition but, as Ringrose points out, 'when toxæmia occurs, the beneficial effects of rest, sedation and delivery are well established'. Is it possible that it is not the drugs *per se* but the confidence they kindle which produces clinical improvement?

Antibiotics for Oysters

'As techniques improve, chemicals will have an increasingly important part to play in the industry's development'. The 'industry' in question is oyster culture and, judging from the article from which the quotation is taken, the modern oyster runs almost the entire gamut of chemotherapy before he tickles the palate of the gourmet. The authors of the article, G. D. Waugh and D. A. Hancock (*Chem. and Drugg.*, 1961, **175**, 667) provide a fascinating account of what is involved today in tending an oyster during the five years that elapse between the free swimming larva settling to the bottom and the appearance of the oyster on the gourmet's plate. Three processes are involved.

The first is the protection of the oyster against 'the ravages of predators and pests' and 'competition from other species'. Here the measures used run from DDT to saturated solution of common salt, quicklime, phenol and copper sulphate. Perhaps the most interesting of these is the use of DDT. This is to control 'the immigrant New Zealand barnacle', *Elminius*

modestus, which has become a serious pest of east-coast oyster-grounds since it first appeared over here in 1945. It settles on the oyster growth surfaces at a rate of 600 per square inch per week in midsummer and thereby prevents the free-swimming oyster larvæ from settling. The second process is that carried out for the sake of the consumer—the purification of the oyster. This is still done by the old-fashioned method of adding chlorine to the water and then letting the oysters cleanse themselves. In inland areas this may be supplemented by ultra-violet light. The third, and newest, process is the use of antibiotics in the artificial rearing of oyster larvæ, which is now being used to help in maintaining a steady supply. Unfortunately, bacterial contamination of the larvæ hatcheries is a common and serious risk, but this hazard can apparently be controlled by 'the judicious use' of penicillin and streptomycin. With the aid of this 'antibiotic umbrella' the survival rate of larvæ has been raised from 10 to over 50 per cent.

Abortion and the Iron Curtain

In a report of an international conference on abortion problems and abortion control held in East Germany last year, C. Tietze and H. Lehfeldt (*J. Amer. med. Ass.*, 1961, **175**, 1149) provide one of the most comprehensive reviews yet published on legal abortion in Eastern Europe. Legislation permitting abortion at the request of the pregnant woman, or on social indications, has been enacted since 1955 in most countries of Eastern Europe. Abortion is prohibited in pregnancies of more than three months' duration, except for medical reasons. It is also forbidden if the applicant has undergone an induced abortion during the preceding six months. The operation must be performed by 'physicians' in appropriately staffed and equipped hospitals and interruption of pregnancy by unauthorized persons or in unauthorized circumstances (e.g. in a doctor's surgery) is a punishable offence. On the other hand, the woman who induces an abortion on herself, or on whom it is performed, does not face prosecution.

According to this report, 'the new legislation has resulted in spectacular increases in the incidence of legal abortion throughout Eastern Europe', and there is evidence that the total number of criminal abortions has 'declined substantially'. The most detailed figures are those from Hungary and these show that in 1959 there were more legal abortions than live births. The only country in which there was no increase was Eastern Germany, where there was a decrease from about 7000 in 1950 to an annual average of about 1000 in 1956-59. One of the many interesting points brought out by this report is the remarkably low mortality rate: 6 per 100,000, for instance, in Hungary. As is noted, this 'compares favourably with mortality from all complications of pregnancy, childbirth, and the puerperium (excluding abortion) in the United States and other advanced countries'. This low mortality rate is attributed to the fact that abortion is performed during the first three months of pregnancy. One of the other many interesting points in the report is that the number of known pregnancies 'increased markedly after the legislation of abortion for non-medical reasons'.

THE PROBLEM OF OBESITY

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THE family doctor who achieves complete success in his efforts to maintain his patients at desirable weight levels has done far more to reduce mortality and morbidity in his community than could be expected from any other kind of health programme.

MORTALITY AND MORBIDITY IN THE OBESE

Food addiction is one of the leading health hazards of modern urban societies. With the exception, so far as is known, of cancer, all the major causes of adult mortality and morbidity are adversely affected by obesity to an important degree. Even the risk of suicide is so influenced. To bring this home to patients it is useful to tell them that if the expectation of life in ten fat and ten thin, but otherwise healthy, people, aged 30, is compared, nine of the thin ones can expect to survive to 60, compared with only six of the fat. It is probably true that for every 10 pounds (4.5 kg.) overweight there is an increase above the average death rate of about 8 per cent., or perhaps more, whereas with 20 pounds (9 kg.) overweight the death rate increases by 18 per cent., with 30 pounds (13.5 kg.) overweight by 28 per cent., and by 56 per cent. when the excess is 50 pounds (22.7 kg.)—and it should be kept clearly in mind that such an excess is commonplace. It is difficult to find any of the commoner important hazards to health and life which do not show an equally severe loading against the obese. Even a fatal accident is about 12 per cent. more common in them and, of course, surgical treatment is more risky directly in proportion to the degree of obesity. In cardiovascular and renal diseases, and diabetes mellitus, mortality is more than twice that in individuals of normal weight, and the incidence of these diseases is much increased in the obese.

FOOD INTAKE OF FAT PEOPLE

It is familiar experience to hear the fat deny excessive food intake, and many will claim that their appetite is small. In examining these views it is not right to start with the idea that the obese are invariably liars. They are all inaccurate in these statements, but there are many subtleties in the situation which need to be explained to patients. Experiments have been made allowing obese subjects freedom to choose and eat their meals under laboratory conditions.

One such study of eight patients asked to eat what they would normally choose at home showed calorie intakes ranging between 1,450 and 3,690, and averaging 2,570. These levels of food intake can scarcely be called small, but when it is observed that in the four-day period of this experiment there was also an average

weight loss of 2 pounds (900 grammes), the normal home intake can be predicted. The details of these results are also interesting; the patient whose measured intake was 1,450 calories weighed 207 pounds (94 kg.) and lost 4 pounds (1.8 kg.) in four days, whilst the one with the largest intake weighed 359 pounds (163 kg.) and lost 5 pounds (2.3 kg.) in this time.

Further evidence of how large the actual intake is in the obese comes from another study of six women allowed an intake of 2,510 calories daily for eighty-eight days; an average weight loss of 2.3 pounds (1 kg.) a week was recorded.

How, then, can one believe either statement under discussion? First, the heavier the person, the greater is the calorie intake required to maintain a given weight level, since the metabolic requirement is not, as is commonly thought, decreased but is increased. Secondly, all these patients have greater or lesser psychogenic preoccupations, and are little conscious of how often they eat small amounts of what is often highly concentrated food. Third, the rate of increase in food intake is often imperceptible and is seldom truly abrupt except in maternal obesity, but here again the mother is preoccupied, is apt to assume, if lactating, that it is her duty to eat excessively and, when lactation ceases, continues to take an increased amount of food, although now on an intake intermediate between her normal and the pregnancy or early post-pregnancy levels.

Alcohol.—Consideration of the intake of alcohol is important in the treatment of obesity in several ways. It is, of course, a source of readily available calories. A pint (570 ml.) of beer drunk slowly yields nearly its potential content of 300 calories, the amount lost depending upon the rate of drinking and hence the rate of excretion. For most, alcohol is an apéritif; for most, even in small quantities, it interferes with judgment and self-restraint. Those who take it daily will seldom follow their reducing programme faithfully. In a prosperous society its consumption is increasing rapidly, and its misuse is increasing with increasing tolerance of moderate consumption. Chronic alcoholism is increasing in most urban societies, and is often unnoticed and unsuspected until catastrophic deterioration follows failure of food intake from gastritis or intercurrent illness, so that many relatively young people, both male and female, have a daily intake of several 'short' drinks twice a day and are not thought of as alcoholics. The misuse of alcohol is a direct effect of psychogenic influences, usually with a background of inferiority feelings and of fatigue secondary to the unending inefficient pursuit of increased status and economic advantage.

The taking of alcohol has therefore a profound effect on obesity. Further, the calorie value of cocktail 'snacks' is considerable: an ounce (28 g.) of cheese straws produces 170 calories, whilst little sausage rolls come out at 140 calories an ounce and this in small bulk. When the intake of alcohol is really considerable, the basal calorie requirements may be exceeded from this source alone. That alcohol should be so important in obesity is hardly surprising. Addiction to most drugs is more a matter of the person than the drug, so that one should anticipate that addiction to alcohol would commonly accompany addiction to food, to so-called weight-reducing drugs or appetite suppressants, and to cigarettes. When such a subject decides

from fear of bronchial cancer or other reasons to try to wean from cigarette addiction, commonly food addiction becomes more severe, and this is a matter which has to be noted in treatment.

NON-DIETETIC FACTORS IN OBESITY

Genetic factors.—There is much evidence to suggest that on occasion inherited factors are important elements in the production of obesity. That intermediary metabolism is in some respects abnormal in the obese seems established; it may be that a genetic background always determines the ease with which obesity may be produced. However this may be, there is no possible genetic structure which can defeat the laws of thermodynamics and enable obesity to appear without a corresponding excess food intake.

Endocrine factors.—There are few endocrine factors in obesity, and the occasional claims that some endocrine preparation or other has produced weight loss are uncritical and untrue. The accumulation of fat about the breasts, pubis, hips, and buttocks in eunuchs clearly has an endocrine origin, and the increase in weight many mothers show in pregnancy and particularly after childbirth may well be due to temporary endocrine dysfunction, and this is the only situation in which an endocrine factor, albeit temporary, is commonly important. The role of the menopause in producing obesity depends on factors similar to those which obtain when weight increases are found to continue after pregnancy. Here, however, there is no evidence of a primary endocrine stimulation of appetite. It is the secondary factors just enumerated which are responsible. It will thus be seen that all so-called endocrine obesity is, in fact, obesity from eating too much, as is all other obesity.

The thyroid in obesity.—There are two great popular misconceptions about the place of thyroid metabolism and thyroid extract in obesity. In the first place it is commonly believed that the myxœdematous are obese. In fact when a large series of patients with primary myxœdema were examined, a third were found to be under standard weight for their height, and only about 60 per cent. were of either normal or above-normal weight. When one remembers that some (and usually most if not all) of the excess weight in those above normal weight is due to the deposition of myxœdematous tissue, then it is the more clear that thyroid deficiency as such, even when advanced, is never a cause of increase in fat storage. Indeed, it is unusual to find a patient with myxœdema who is grossly obese. Even in the overweight patients with myxœdema the rapid weight loss when given thyroid extract has been shown to be due to the loss of the abnormal tissue, and not to the loss of fat. It is almost certainly true that in all hypothyroid states the amount of stored fat diminishes. That the exhibition of thyroid extracts to obese patients can help in any way to increase metabolism in a beneficial fashion is completely untrue. It should be regarded as grossly improper treatment since its only effects are adverse and no weight loss can be produced by its use without simultaneous intoxication from it.

FAT STORAGE IN THE OBESE

Fat is stored in cells in the main mesodermal mass which may be regarded as specific cells of the reticulo-endothelial system. Fat can thus be considered to be treated as foreign material and to be dealt with by the body scavenging department. In their embryonic state the cells concerned have a glandular structure, and assume their familiar adult form only as they become distended with fat.

The storage of fat appears to be an active metabolic process but even if the intake of fat is below the energy requirements of an animal, virtually all the fat intake seems to be deposited in the fat tissues. Under some experimental conditions there is a parallel increase in the blood fat levels corresponding with diminution in the amount of fatty tissue in the body. It is likely that carbohydrate is the main precursor of fat. The effects of diets of the same calorie content but differing constitution are important.

Studying obese patients on 1000 calorie diets with a fixed water and salt intake, Kekwick and Pawan found that weight loss was most rapid when the carbohydrate content for the diet was minimal, and most rapid on a high-fat diet. Further, such patients excreted greater amounts of a 'fat-mobilizing substance' in their urine when on a high-fat 1000 calorie diet than when on a high-carbohydrate 1000 calorie diet, whereas normal subjects excrete large amounts of this material when completely deprived of food. They have also shown that it is much more difficult to induce ketosis in obese than in normal subjects and it would seem that the rate of production of ketone bodies is lower in the obese since the rate of disappearance of sodium β-hydroxybutyrate from the blood after intravenous injection was the same in obese and in non-obese subjects. In both groups the same amount—less than 1 per cent. of the injected dose—appeared in the urine. They explain their results by pointing out that in normal people on a high-fat diet a fall in fasting blood-sugar levels precedes the appearance of ketone bodies in the blood and ketosis, whilst in obese subjects on a similar diet no such fall or only a small fall was observed, and they did not develop ketosis to any appreciable extent. Their interpretation is that there is a net conversion of fat to carbohydrate in both groups, but the obese may be able to turn fat into carbohydrate at a higher rate than normal subjects.

In mice they found that the injection of a urinary extract from fasting human subjects produces weight loss not obtained in controls given either saline injections, or urinary extracts from people on normal diets, even when the food intake of the two sets of human subjects is the same.

The existence of such a 'fat-mobilizing substance' would bring our concept of how the 'adipose organ', as Kekwick calls the fatty tissues, is controlled, much nearer our ideas of how, for example, insulin exerts its profound control over carbohydrate metabolism. One naturally speculates at once whether purification and concentration of such an extract will provide the answer to fat people's prayers. In the present state of knowledge this must remain a speculation, although one's instinct would suggest that a substance having so potent a metabolic activity is very unlikely not to possess dangerous side-effects when used in non-physiological doses. Further development of this work, however, remains one of the most exciting pieces of present-day investigation.

This material is not the only substance known to increase, at least *in vitro*, the rate of liberation of free fatty acids from fatty tissues: adrenaline,

noradrenaline, corticotrophin and growth hormone have these properties, but none of these has any potential place in the treatment of obesity.

TREATMENT

Diet is the essence of treatment and its control requires particular thought. The use of printed diet sheets is not the ideal method. Patients are individuals, and quite properly like to be so considered. In the treatment of obesity each patient requires some specific individual instruction. It is a small matter to add the patient's name at the head of the diet sheet, but this simple measure gives many patients the idea that this is something for themselves. If printed sheets are used a space should always be left for the insertion of individual instructions.

The following dietetic instructions have proved successful:—

DO NOT EAT **AT ALL**

Bread (and this means also all its substitutes)
Sugar
Sweets
Chocolates
Cakes
Pastries
Puddings
Potatoes

Common bread substitutes:
Biscuits, Energen, Ryvita, Procea, toast, brown and all 'starch-reduced' breads.
None of these is allowed.

EAT IN MODERATION: **SMALL HELPINGS ONLY**

Lean meat
Fish
Vegetables (except potatoes)
Fruit
Poultry
Game
Cheese
Eggs

Do not take more than 2½ pints (1.5 litres) of liquid a day. Clear soups are allowed, but thick soups and sauces must be avoided. Take as little salt as possible.

Fat should be cut down to a minimum and the fatty parts of helpings of meat avoided. Rich fat fish such as herrings, salmon, and halibut should be taken only in small quantities.

Take salads and vegetables in really small amounts. Whilst there is very little food value in salads and green vegetables, their consumption in considerable amounts will make dieting extremely difficult since eating anything in bulk has an effect in promoting appetite.

Alternative additional directions suitable for different patients are as follows:—

(1) For all generally fit people it is wise to add a paragraph such as:—Take increasing amounts of walking or other exercise which suits you, as the dieting proceeds. This gives some slight help in making you lose weight a little faster but it is also important for general fitness to try to take at least some walking exercise daily.

(2) If there is some general disability such as cardiac or respiratory insufficiency, the following paragraph is indicated:—As your weight goes down, you may find it comfortable to walk a little more daily. If you can do this without bringing on uncomfortable symptoms, the exercise will be helpful and will contribute a little to the speed of weight reduction.

(3) When the patient takes alcohol it is most important to include a prohibition which should, according to circumstances, either be absolute or there should be a statement of the amount permitted as a maximum. Some would add the pro-

hibition of alcohol to the general dietetic directions for all patients. It seems pointless to do this if the patient is a teetotaller, and in such instances gives an impression that other aspects of the diet are not really intended for this individual.

It will be noted that there is a partial prohibition of the use of fat in the standard diet directions. This may be questioned in that the rate of weight loss is higher on a high-fat diet than on any other diet of equal calorie content. Since in prescribing a diet one wants to make it as certain as possible that the patient not only can, but will, stick to the directions, it is important to note that a high-fat diet is not acceptable to many, and it is difficult to arrange.

Some patients like to have their lives ordered in great detail, and there are often requests for a diet sheet which lays down precise amounts of food. Occasionally it is useful to give the directions in this form, and then the following instructions may be used:—

REDUCING DIET—*Day's rations*

1 egg
2 whites of egg
¼ ounce (7 g.) butter
4 ounces (113 g.) lean meat, fish, or poultry
12 ounces (340 g.) of vegetables*
3 ounces (85 g.) of fruit†
¾ pint of skim-milk
2 helpings of clear soup or broth

Arranged as:—

Breakfast—part of fruit allowance, one egg with two egg whites scrambled, part of butter ration used in egg dish, part of skim-milk ration, with tea or coffee.
Dinner and *Supper*—one cup clear soup or broth, lean meat, fish or poultry, 6 ounces (170 g.) vegetables, remainder of skim-milk ration.
No snacks.

* All vegetables do not contain the same amount of starch. Potatoes, baked beans, and indian corn contain too much to be allowed at all. If green peas or parsnips or jerusalem artichokes are taken, the ration should be reduced a little. All other vegetables can be treated as of similar starch content.

† All fresh fruit in the stated quantity except banana and cherries.

In general, a really low calorie diet is much easier for the patient after the first few agonizing days, than one of 1000 or more calories. It is true that most patients will lose weight slowly over a long period on a 1000-calorie diet, but the results are not very quickly evident and small departures from the strict regime are much more rapidly significant. It is always worth while trying to explain to patients this one essential point—that after a few days hunger will diminish if the regime is maintained without any variation.

Rate of weight loss on diet.—There is seldom a uniform and steady weight loss on diet. Most patients find that the loss is most marked at the beginning of their campaign. Much of the variation is really due to lack of faithfulness in sticking to the diet, some is due to variations, often considerable, in physical activity in different weeks. There are, nevertheless, other factors. The greater the weight loss achieved, the less the food intake necessary to maintain a given weight level. Unless therefore considerable increases in physical activity accompany the improvement in weight, food intake has to be decreased very slowly but progressively to maintain the same rate of loss uniformly. The daily fluctuations in normal weight are substantial. It can be

predicted that morning weights will be less normally than evening weights, since there is normally no nocturnal food intake while basal metabolic requirements are still to be met. Weight varies also from other simple causes: e.g. the bladder may hold a pound of water without effort, and a meal before digestion may weigh two or more pounds (900 g. or more). The watery bowel evacuation after a laxative may represent a weight loss of several pounds of water. In the obese the daily swing seems often to be greater than those found in normal subjects, and disturbances of water storage appear to be associated with obesity. Indeed careful studies have demonstrated that to some extent periods of unexpectedly large weight decreases during dietetic treatment may be due to increased water loss, and periods, sometimes prolonged, of weight maintenance while a reducing diet has been followed faithfully, may be due to increased water storage.

When discussing the advisability of exercise in treatment, it is necessary to advise great caution in the rate of increase in exercise as weight reduction proceeds. Some will become comfortably active again and should be encouraged to continue this mode of life, but for many, if not most, at least after early middle age, exercise more violent than golf should not be taken up again until a substantial period of normal health and weight with regular walking exercise has demonstrated the absence of damage from previous obesity. Such advice is the more important since the dividends in weight loss from increasing exercise are so poor compared with those from tackling the main cause, overeating. Whilst exercise proper and safe for the patient is to be encouraged, it must be made clear how surprisingly small the fuel requirements of even violent exercise turn out to be.

Complications in the course of treatment.—The main complication met with when a patient follows a reducing regime seriously is the appearance or increase of constipation. This is a serious matter for many, and should never be dismissed as unimportant, since the discomfort, actual and psychological, may make it impossible for the patient to continue to diet. Usually the prescription of a bulk-producing laxative is effective. Sometimes a combination of one of these with a preparation such as 'senokot' is more satisfactory. Sometimes it is necessary to increase the fluid allowance, and add a few prunes—despite the relatively high carbohydrate content—to the diet. Many will be concerned lest they be deprived of necessary vitamins and other essential food factors. In this country, at any rate, the diets suggested will always provide a sufficient quantity of all essential factors, but there is no harm in the winter months in adding a mixed vitamin supplement and, even if this sort of preparation is used as a placebo, its cost is trifling compared with the national benefit to be obtained from effective weight reduction.

THE USE OF DRUGS

As the control of appetite is the main essential to success in treatment, it has seemed logical to seek a drug with an appetite-suppressant action, and many products are claimed to have such effects. Of these, amphetamine and

its relatives are those most commonly used. In a busy surgery, with a queue of other patients waiting, it is obviously easier to prescribe some tablets than to attempt to discuss the etiology of obesity. There is no evidence, however, that the prescription of amphetamine and its relatives has any but a short-term effect on the control of appetite. No considerable series of patients studied over a reasonable period has shown benefit in weight reduction from their use. These are dangerous drugs of addiction, and to treat food addiction with such drugs is totally illogical. In my experience, those doctors who prescribe most of these drugs spend least time in discussion with their patients; they are also, as a rule, those who show the least evidence of general professional competence. These are harsh words, but the treatment of obesity is so essential to the public health in our society, that they are justified if they help towards a more enlightened viewpoint.

This does not mean that no drug has any place in the treatment of obesity. It is often wise to use mild sedation in the first two to three weeks of treatment, to tide the patient over the first period of dieting, when irritability is often considerable, and often aggravated by the jocular or stupid or other unhelpful remarks of friends and family. Further, if an attempt at superficial psychotherapy has been made, some mild sedative adjuvant is sometimes especially helpful. Of available sedatives, none is superior to phenobarbitone or amylobarbitone. The newer sedatives and so-called tranquillizers have too many disadvantages for it to be worth while exploring their effect on an individual patient in this sort of situation. On the other hand, to prescribe ½ grain (30 mg.) of phenobarbitone or 1 grain (60 mg.) of amylobarbitone two or three times a day for the first weeks of dieting may prove of potent help. Food addiction is so chronic a disorder when treatment is first attempted that it is unusual for withdrawal to be successful unless helped in this way.

PSYCHOGENIC INFLUENCES

Gross psychogenic influences are by no means of uniform importance in every patient who is obese. For all practical purposes, however, such factors are predominant in all cases of gross obesity, and in the majority of children and young people who are obese. Neurotic elements of importance are absent in but few fat people. Many will have realized that their normal reaction to worry or upset is to take a cup of tea and a snack more often, or that they have to eat almost compulsively, or that they take more alcohol under such conditions, and these reactions are often scarcely outside the limits of normal human responses. When this response ceases to be occasional and becomes habitual, the severity of the underlying psychopathology is usually substantial.

Investigation of the results obtained in differing approaches to the treatment of obesity has shown uniformly consistent results.

For example, a group of 93 people was divided into four groups: 38 were treated by superficial psychotherapy and explanation of the simple facts of food values and energy exchange, without the provision of calculated diet sheets and without drugs. A second group of 35 patients was given an 800-calorie calculated diet

which was explained to them by an experienced dietitian and further instructions were given on demand during return visits, but no psychotherapy was provided and no drugs. Ten patients were given 5 mg. of amphetamine three times a day without psychotherapy and without a calculated diet, whilst the fourth group was given thyroid extract in place of amphetamine. All the patients under study proved to have varying degrees of neurotic difficulty. The best results were obtained in the first group, and the conclusion was reached that both psychotherapy and return to proper food habits are essential to maximum therapeutic success. No other treatment produced regular permanent success.

Expert psychiatric knowledge is by no means essential for quite successful, if superficial, approaches to psychotherapy, and it is wise in any event to leave discussions of matters not obviously connected with weight and diet until a careful and sympathetic approach to these items brings a comfortable assurance to the patient that the problem is going to be considered both seriously and kindly. Parading the psychological aspect is to court therapeutic disaster almost as certainly as ignoring it. To encourage the patient to discuss the periods of upbringing and development, noting important conflicts in essential spheres of adjustment, and particularly correlating coincidences in times of periods of stress and strain and the appearance of weight changes, will usually provide a sufficient initial ventilation of anxieties and conflicts. As one gradually gets to understand the fears and hopes, ideas and ambitions, failures and desires in emotional relationships one will seldom have failed to produce improvement simply by not only allowing, but encouraging, the patient to talk about himself and the ordinary everyday happenings and problems he has encountered, and such a conversation will often prove to have been the first real period of self-expression the patient may have experienced. As a rule, little is really required beyond listening with sympathy, and from time to time making a remark or asking a question to enable someone who is often not normally articulate about deeply felt feelings and aims, to continue to explore the situations in life which have disturbed or disappointed him. It is the self-revelation so produced which is therapeutic.

Group therapy.—When, with sufficient interest in psychiatric training in this country, enough people become available to provide properly controlled group therapy, it would seem that this form of treatment may have a useful part to play in the treatment of obesity. Studies made so far indicate that what is to be expected from group treatment is not so much an accelerated rate of weight loss, but rather better results in maintaining weight loss once this has been partially or fully achieved. This is an important aspect of treatment since many will lose 14 pounds (6 kg.) or more in weight and then revert to their normal eating habits, losing thereby what, after all, has been a substantial personal effort. In group studies this kind of relapse has been prevented in about 50 per cent. of groups consisting of patients chosen because of difficulties of this kind—a success rate of significant order in so difficult a therapeutic situation. The simplest kind of group treatment is a lecture in which simple explanations of the origin and mechanism of symptoms is given.

FATTY ACIDS AND CORONARY DISEASE

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For the last five or six years there has been a great deal of noisy discussion concerning the role which dietary fat may play in the causation of ischæmic heart disease (I.H.D.). In particular, the theory has been forcefully propounded that the disease is brought about chiefly, if not entirely, by a deficiency of essential fatty acids (E.F.A.). These are unsaturated fatty acids with at least two double bonds and certain other features. The commonest is linoleic acid, which occurs in many of the liquid vegetable oils like maize oil. Most animal fats consist chiefly of saturated fats and have a very small amount of E.F.A., but oils from the whale are relatively rich in E.F.A. When whale and vegetable oils are hydrogenated to make solid fats such as margarine, the amount of E.F.A. is considerably reduced.

I propose to examine the evidence for the suggestion that ischæmic heart disease is due to a dietary deficiency of essential fatty acids. I shall do this by testing the evidence against the same criteria which have been used for other dietary deficiencies: for example, in deciding that beri-beri is primarily due to a deficiency of aneurine.

DIAGNOSTIC CRITERIA OF NUTRITIONAL DEFICIENCY

(1) There should be evidence of nutritional deficiency. This deficiency may be primary, as when we find that the diets of many of those who develop beri-beri are low in aneurine. Or the deficiency may be secondary or conditioned; here the intake may normally be adequate, but becomes inadequate because of factors which increase requirements. Thus, some people do not develop beri-beri on a marginal intake of aneurine, but do so when they undertake heavy physical work for which they require more aneurine than normally.

(2) The signs and symptoms should be those which are found in the specific deficiency. Evidence may come from animal experiment, or from clinical and laboratory tests in man. It was observations on chickens fed with polished rice which gave the first clue that beri-beri was of nutritional origin. Patients with the disease have a decreased amount of aneurine and an increased amount of pyruvic acid in the blood and urine, as was forecast by those working on the biochemical functions of aneurine.

(3) The third criterion is that the condition should be prevented or cured when the deficiency is made good. Œdema and heart failure in wet beri-beri improve with remarkable rapidity when aneurine is given; this has been used in times of famine to differentiate wet beri-beri from hunger œdema.

It sometimes happens that all the criteria cannot be met. For example, the paralysis of long-lasting chronic beri-beri may not be completely reversible, because of the death of some of the nerve cells. Nevertheless, in searching for the etiology of disease, one should seek evidence to meet all the criteria; conclusions should then be drawn only from weighing the total evidence.

SOME BASIC MISUNDERSTANDINGS

Before the etiology of I.H.D. is discussed it is necessary to straighten out some of the confusion which has been introduced into the subject.

I.H.D. in the form of either angina pectoris or myocardial infarction is due to chronic or acute obstruction of the lumen of the coronary arteries. The narrowing occurs in vessels which are affected by atherosclerosis. Thus, it is correct to say that I.H.D. cannot occur without atherosclerosis, but it is wrong to say that the cause of the one must be identical with the cause of the other. In the first place, extensive atherosclerosis can occur in the aorta and other parts of the arterial tree, with little or none in the coronary vessels. Secondly, a small localized but severe lesion in the coronary arteries may lead to occlusion, whilst far more widespread lesions may exist in the coronary arteries without the development of occlusion. Thirdly, atherosclerosis exists in varying degrees in almost all adults in this country; it is, however, usually impossible to determine its existence, and always impossible to discover its extent, except at necropsy.

From these facts, it follows that we cannot take the incidence of I.H.D. as a measure of the incidence of atherosclerosis. When we come, then, to discuss the evidence concerning etiology, we must take care to differentiate between the etiology of atherosclerosis, and the etiology of I.H.D.

EVIDENCE OF NUTRITIONAL DEFICIENCY

Here we ask the question: can we demonstrate that those who develop I.H.D. have a diet deficient in E.F.A.? Further, since there is evidence from animal experiment that E.F.A. requirements are increased when the intake of saturated fat is increased, we may also ask whether there is evidence of a high intake of saturated fats among those who develop I.H.D.

It should be said at once that there is no evidence at all concerning the individual diets of those who do, or do not, develop the disease. The only evidence which exists is derived from epidemiological studies. We can compare, that is, the average diet of groups of subjects with the incidence of I.H.D. in those groups. In reviewing the information on this point, however, it must be noted that the accuracy of information, both as to diets and as to incidence, is often highly suspect.

In the first place, groups of people may be compared over a period of time: that is, in one country the changes in incidence of I.H.D. may be compared with the changes in diet. Here, too, we must keep clear in our minds the distinction between atherosclerosis and I.H.D. There is evidence that in Britain over the last fifty years there has been no increase in the

incidence of atherosclerosis, although most people are agreed that there has been a great increase in the incidence of I.H.D. During the same period there is no evidence of a decrease in E.F.A.; there was probably in fact an increase. For part of the time, it is true, there was an increase in total fat, but this fell for several years during the period of rationing. During the same period, there was a twofold increase in the number of people recorded as having died each year of coronary occlusion. As I have previously reported, in Britain from 1928 the closest relationship with reported changes in mortality due to coronary disease was shown by the number of licences issued for radio and television.

It is often said that the experiences in Scandinavian countries during the 1939-45 War reveal a relationship between coronary deaths and dietary fat. A close examination of the published figures does not support this conclusion. For example, the most commonly cited figures report mortality from 1935 to about 1947 from all forms of arteriosclerotic disease and not only coronary occlusion; they are related to consumption of butter, milk and eggs, and not to that of total fat. More important, however, they by no means show the consistent association between mortality and diet which is often claimed.

For example, Denmark's fat consumption was steady before the war, then fell to one-half between 1940 and 1947. Mortality was almost constant from 1935 to 1948, except for a rise in 1946 and 1947. Sweden's fat consumption, except for a moderate fall in 1941 to 1943, was fairly steady for the whole period. In spite of this, the mortality from arteriosclerosis rose from 1935 to 1940, fell to 1942, and then rose again from 1942 to 1947.

Other epidemiological evidence comes from comparing diets and disease in different populations at the same time. Partly, this has been done from international statistics: of coronary deaths given by WHO, and of dietary components given by F.A.O. The results show that, in very general terms, the greater the fat intake, the higher the coronary mortality. But there are many exceptions, and the results are no better if one attempts to differentiate between saturated fats and unsaturated fats. At least as good a correlation exists between coronary deaths and consumption of animal protein or consumption of sugar.

Several studies, notably by J. N. Morris, have been made on other groups, defined by occupation, geography or economic class. Most of the results do not support a simple dietary cause of I.H.D. In Britain, mortality statistics show that general practitioners are much more likely to die of I.H.D. than consultants; farm workers than town workers; building labourers than dock labourers. It is difficult to imagine that there are differences in the intake of E.F.A. or of saturated fat which could account for these differences in mortality. In the United States, in Britain, and in some other countries, there are quite large regional differences in the incidence of I.H.D. For example, it is higher in Scotland than in England and Wales. There are also differences in diet, but these are slight and show a *lower* intake of fat in Scotland. In the United States, it has been claimed

that the appreciable differences in incidence of I.H.D. between states is quite unrelated to differences in diet but *is* related to the degree of hardness of local water.

Statistics in Britain show appreciable differences in coronary mortality between the different economic classes. Professional workers have twice the chance of dying from I.H.D. as the semi-skilled and unskilled workers. What information is available reveals very little difference in the diets of these different classes. More direct studies between different groups have also been made, by observation rather than from published statistics. Such studies often show a dissociation between atherosclerosis and I.H.D. For example, Jamaicans and Japanese, with low intakes of fat, have a low incidence of I.H.D., but are said to have as much atherosclerosis as white Americans. American negroes have a lower incidence of I.H.D. than white Americans, but a higher degree of atherosclerosis. There is still some discussion whether the South African Bantu has much or little atherosclerosis, although it seems he eats little fat and has little I.H.D.

As regards I.H.D. itself, we find that its association with consumption of saturated fats is by no means universal. In Kenya, it has been found that Indians originally from around Bombay, and others originally from Punjab, keep closely to their home diets. The former eat little fat, mostly of vegetable origin, and the latter eat more fat which is mostly of animal origin. Yet there is no difference in the incidence of I.H.D., which is low in both groups. Another example is provided by the Yemenite Jews in Israel. Those who have lived in Israel for twenty years or more have a risk of developing I.H.D. which approaches that of the Jews from Western countries, who in turn have the high risk of the populations of those countries. On the other hand, the recent immigrants from the Yemen have a very low risk indeed. This is important, for the increased incidence during the years of their stay in Israel might be due to the change from the diet in the Yemen to the Western European type of diet eaten in Israel. Earlier reports that the diet in the Yemen was low in fat, and that this was mostly vegetable oils, have recently been shown to be based on misleading surveys carried out in Israel during a period of severe rationing. It has now been found that the food eaten in the Yemen has quite a moderate amount of fat, and that by far the larger part of this is butter and mutton fat.

Most of the comparisons which have been made between groups, of which only a few have been quoted, have the disadvantage that they are made between groups in which possible differences in diet are accompanied by differences in other conditions. The Japanese differ from the Americans not only in the food they eat, but in the clothes they wear, in the jobs they do and in the ways they relax from their jobs. It is not often that we can find groups in which there are similar living conditions but different diets, or, alternatively, groups in which there are different living conditions but similar diets. There are, however, two recent studies, one of each sort, which are relevant to our discussion.

One study examines the records of deaths due to coronary occlusion in a communal settlement (Kibbutz) in Israel. Here, all members eat the same sort of food in a communal dining-room. Thus, all should equally have been potential candidates for I.H.D. This was not so; those members who carried out clerical and other sedentary jobs were twice as likely to develop the disease as those doing agricultural and other work requiring physical exertion.

The second study is one in which living conditions were very similar, but the diets significantly different. It was carried out in Holland on a group of Benedictine monks and a group of Trappist monks. Both led similar, austere and physically fairly active lives. The Benedictines ate a diet very much like that eaten by the ordinary Dutch population. The Trappists ate a diet which was mostly vegetarian. It contained little animal fat, from milk and cheese; most of the fat was of vegetable origin. Nevertheless, the incidence of I.H.D. was almost exactly similar in both groups, and much lower than in the general population. There was only one case of clinical coronary infarction, confirmed by electrocardiogram, and this was in a Trappist. Of the monks over 60 years of age, electrocardiographic examination showed bundle branch block and other signs of previous small infarcts in the same proportion, 40 per cent., in both groups.

We must conclude, then, that there are many difficulties in the way of accepting the epidemiological evidence as supporting the hypothesis linking deficiency of E.F.A. with I.H.D. Most of the evidence is derived from uncertain information, makes comparisons between groups in which diet is only one of many variables, and in any event does not constantly show a relationship between dietary fat and I.H.D. There is only little evidence from situations where the variables are reduced sufficiently to allow more certain deductions; what emerges from this evidence certainly does not support the hypothesis.

EVIDENCE FROM EXPERIMENTAL ANIMALS

Understandably, and with good cause, a great deal of experimental work is being done with animals in an attempt to throw light on the cause of I.H.D. in man. It is, of course, essential to interpret such results with caution. It is clearly impossible to summarize the hundreds of reports which appear every year, so that I have of necessity to be selective. An added difficulty is that the findings of some workers are contradicted by those of other workers.

So far, the only thrombotic lesions which have been produced in animals are quite different from coronary occlusion in man, and require drastic and elaborate alterations of diet together with the administration of substances such as thiouracil and cholic acid. Their relevance to the human situation is thus too remote for worth-while comment. Most of the experiments with animals have been concerned with the production of atherosclerosis. This work has usually been done in rabbits, chickens and rats. The earlier work consisted of feeding large amounts of cholesterol, but more recently lesions have been produced by alteration only in the quantity and quality of the fat.

Rabbits develop fatty lesions of the arterial intima when their diet contains 3 per cent. cholesterol. The addition of corn oil reduces this. This finding, however, is less impressive than superficially appears; the cholesterol alone increases the incidence of the intimal lesions by a factor of about forty, and

the reduction achieved by the addition of corn oil is only about 30 per cent., still leaving the incidence of lesions some thirty times more than in the control animals. In some experimental conditions, fatty lesions may be produced in the arterial intima of rats, as well as in that of rabbits, by the addition of ground-nut oil, which is relatively rich in E.F.A.; butter does not produce these lesions though it does produce massive intravascular thrombosis.

It has been argued, very reasonably, that the lesions produced by these experimental techniques are probably quite different from those occurring spontaneously in man. For this reason, it is interesting to see the effects of dietary change on the spontaneous lesions which occur in hens. It has been found that the addition to the diets of even quite large amounts of corn oil for quite long periods has made no difference to the development of the arterial lesions.

The important question of the relation of the conditions produced experimentally in animals to atherosclerosis as it occurs in man requires further consideration. If the lesions are different in their mode of progression, as most pathologists suggest, the possibility must be accepted that they are also different in their pathogenesis. This means that we are liable once again to fall into the trap of false analogy, and it is not irrelevant to recall that there was once in clinical medicine a vogue for treating urinary lithiasis with vitamin A, or muscular dystrophy with vitamin E, since deprivation of these vitamins produced somewhat similar conditions in the experimental animal. The essential fact which emerges from the vast amount of work done with animals is that the signs of experimental E.F.A. deficiency, now known and studied for nearly forty years, have never been shown to include the production of either atherosclerosis or coronary occlusion.

EVIDENCE FROM SIGNS AND SYMPTOMS IN MAN

We know little of the effects of undoubted E.F.A. deficiency in man. Experimental E.F.A. deficiency has been produced in infants, and leads mainly to dermatosis. We have therefore to seek our evidence in reverse, in that we examine the ways in which persons with I.H.D. differ from those without, and then determine whether these differences might have been produced by E.F.A. deficiency. It is clear that such evidence can at best be suggestive and circumstantial, since we do not know what changes are really produced by the deficiency.

The differences that have been sought by investigators reflect the uncertainty of the development of the final lesions in I.H.D. Since atherosclerosis is a necessary—though not a sufficient—condition for the production of I.H.D., much of the work has concerned the possible origin of the changes in the arterial intima. A great deal of time could be spent in discussing whether the atheromatous lesion begins with deposition of fatty material, or with an intimal thrombosis or hæmorrhage. Equally relevant is the role of

thrombolysis: that is, the factors responsible for removing the earliest formed thrombus. It is certain that investigations of this sort are most important to our eventual understanding of atherosclerosis and, through it, of I.H.D. For example, modern biochemical techniques have revealed some interesting features of the chemical make-up of the atheromatous plaques. But the results so far cannot be said to support any hypothesis for the origin of I.H.D.; more accurately, perhaps, the results can be used to support any one of a number of hypotheses.

More must be said about one aspect, which has seized the imagination of both doctors and public, and that is the association of high levels of blood cholesterol with I.H.D. Statistically, such an association exists in that apparently normal persons with elevated cholesterol levels are more likely to develop cardiac infarction. This observation, however, has relevance only in so far as it might be shown that hypercholesterolæmia is a sign of E.F.A. deficiency. But the evidence for this is only slender and indirect. Men fed large amounts of saturated fatty acids show an increase in the level of cholesterol. Men with high levels of cholesterol show a fall when they are fed E.F.A. To this, however, must be added many other observations. The rise in cholesterol can be brought about not only by an increase in dietary saturated fat but also by an increase in carbohydrate and in animal protein, by decrease in exercise, and by mentally stressful situations. The fall from high levels can be brought about not only by dietary E.F.A., but by other unsaturated fats which are not active as essential fatty acid. It can also be brought about by administration of drugs with thyroid activity, by nicotinic acid, by aspirin, by PAS and by magnesium. In view of all this, hypercholesterolæmia cannot be taken as evidence of E.F.A. deficiency.

EVIDENCE FROM THERAPY

The third criterion for the diagnosis of nutritional deficiency is that the condition should be prevented or cured by making good the deficiency. So far, little work has been done on these lines. Moreover, some which has been reported does not clearly show whether it has been adequately controlled. The only well-organized tests are those which have studied, not the prevention of I.H.D. in normal persons, but the prevention of recurrences in persons who have had one confirmed attack of myocardial infarction. The method has been to change the diet of some of the subjects, so that they ate less saturated fat and more E.F.A.-rich fats. In three such studies, which have now proceeded for two years or more, the incidence of recurrent attacks of infarction was no lower in this treated group than in the control group whose diet had not been changed.

It has been suggested that the failure of E.F.A. to prevent recurrence of infarction is not surprising, since the lesion which leads to the first obvious infarction may well by then be irreversible. This would be analogous to the situation where it becomes impossible to improve the paralysis of chronic beri-beri. In this case, we must await acceptable evidence of the prophy-

laxis of I.H.D. by the administration of E.F.A. to apparently healthy people who have had no history of coronary occlusion. Until this is done, it is not unreasonable to say that the onus of proof still lies with those who support the hypothesis that I.H.D. is due to deficiency of E.F.A.

SUMMING UP

The situation may be summarized by saying that the evidence that I.H.D. is due to a nutritional deficiency of particular fatty acids is by no means conclusive. It may even be said that the balance of the evidence is against this hypothesis. In assessing the evidence, we must distinguish between those facts which can be made to fit the theory, and those which apparently contradict it.

To make this a little clearer, let us consider some examples of both sorts of evidence. In its simplest form, the theory relating I.H.D. to the deficiency of E.F.A. would require the demonstration that the disease occurs in those whose diets are low in essential fatty acid. It was evident from an early stage that the existing facts did not fit this direct association. It was necessary to introduce a very reasonable modification to the hypothesis: that E.F.A. deficiency could be precipitated by the increase in requirement when there was an increased intake of saturated fats. Soon, further modifications were necessary—that E.F.A. requirement was increased by a deficient intake of vitamins B_6 and E—and this was used to explain the apparent (though in fact not real) association of the disease with the consumption of white bread. Further modifications were concerned with the alleged (and since disproved) antagonistic action to E.F.A. of 'unnatural' fatty acids produced by hydrogenation of oils to make margarines and shortenings. Again, it was predicted that atheromatous deposits would contain cholesterol combined with saturated fatty acids, rather than with E.F.A.; the opposite is the case, and the theory has accordingly been modified. Perhaps the most important modification of the original theory is that it is no longer held that there is a straight-line relationship from E.F.A. deficiency to hypercholesterolæmia to atherosclerosis to I.H.D.

One of the more far-fetched modifications relates to the difference in coronary mortality in different occupational groups where there is unlikely to be significant differences in diets. This depended on the known influence of the sex hormones, which accounts for the higher mortality in men than in pre-menopausal women. The female hormone is supposed to work by decreasing E.F.A. requirements, so making deficiency more likely in men, and in women after the menopause. The suggestion was then made that bus conductors have a lower incidence of I.H.D. than bus drivers because the conductors are less 'virile'; similarly, medical consultants are supposed to be less 'virile' than general practitioners.

All of these examples, and many more, simply show that it is possible to manipulate the theory in such a way as to accommodate many—perhaps most—of the new facts which have been accumulated since the theory was

first put forward. There remain, however, some facts which seem so directly opposed to the theory that it is difficult to imagine how Procrustes himself could fit the theory to them. Why, for example, is there so little I.H.D. among Benedictine monks, or recent Yemenite immigrants to Israel, or Punjabi Indians in Kenya, when the diets of all these groups are just as deficient in E.F.A. as those of populations with a high incidence of I.H.D.? Or consider animal experiments, where it has been argued that the reason that it is difficult to reverse 'atherosclerosis' by administration of E.F.A. is that it has progressed too far. This suggestion does not explain why the spontaneous lesions in hens are not prevented by even prolonged administration of a diet rich in E.F.A.

Let us return for a moment to the strong probability that in Britain, and possibly other advanced countries, there has been no increase in atheroma but a considerable increase in I.H.D. Either there has been an increase in the incidence of E.F.A. deficiency (primary or secondary), or there has not. If there has, it could perhaps be responsible for the increase in I.H.D., but it could not be responsible for atherosclerosis which has not increased. If there has *not* been an increase in E.F.A. deficiency, then clearly there must be some other cause for the increase in I.H.D.

EPILOGUE

One of the characteristic features of those who nowadays write on the etiology of I.H.D. is that they select the data which they quote. In so far as the data are now so vastly numerous, selection is essential, but it also allows us to pick out those pieces of evidence which support our thesis, and ignore the rest. It is by now obvious that I, too, have been selective in order to prove a thesis. My thesis, however, is not a theory of etiology, but that it is impossible consistently to support any one such theory. It is for this reason that I have mentioned only those pieces of evidence which, I believe, demonstrate that I.H.D. is not a straightforward manifestation of deficiency of E.F.A. It is for this reason, too, that I have stressed the difference between the two classes of evidence which are loosely grouped together as negative; some negative evidence simply does not immediately support the theory, but other negative evidence apparently contradicts it. However many new facts are found which are compatible with the theory, it will not become more acceptable unless it can be made also to explain the contradictions.

The truth is that all the evidence points to a multiple origin of I.H.D. The factors probably include constitutional predisposition, physical activity, mental stress, smoking and overweight. Overweight implies general dietary factors. It may turn out that specific dietary factors are also concerned, and one of these might be deficiency of essential fatty acid. Nevertheless, quite as good a case may be made out for an excess or deficiency of other single nutrients, which also may play some part among the many other factors, dietary and non-dietary.

NUTRITION AND INFECTION

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FAMINE and pestilence still haunt the earth. Infectious diseases still continue to take their highest toll among the underprivileged classes in a community and among the peoples of the underdeveloped countries: that is, wherever malnutrition or undernutrition is most prevalent, or where war, with its severe food restrictions, may lead to an increase in infectious disease in previously well-nourished communities. Much of this epidemiological and clinical evidence, however, can only be suggestive because food in quality and quantity is not the only disturbed factor in such conditions; as a rule a poorly fed community is poorly organized in other respects also. As Howie (1949) pointed out, such a community lacks hospital beds and public health organization to isolate infectious diseases; its members suffer fatigue, anxiety and low morale; they crowd into uncomfortable, often infested, dwellings and their personal hygiene is poor.

SOME INHERENT DIFFICULTIES

Because of the inherent difficulties of interpretation clear definition of the extent to which the nutritional state can affect the resistance of man to infection cannot be provided, and examination of the literature relating nutritional status to infection in lower animals is not much easier to understand. Like human beings, animals in a state of profound nutritional deficiency are highly susceptible to bacterial experimental infections, whilst Boyden and Andersen (1955, 1956), Howie and Porter (1950) and Dubos and Schaedler (1959) have reported that experimental regimens which prove best for growth and reproduction are not necessarily those most favourable for resistance to infection.

The history of tuberculosis in Denmark during the 1914-18 period appears to demonstrate a clear-cut association between a rise in tuberculosis and a decline in food intake without other complicating factors such as actual participation in war. Livestock products were greatly reduced by sales to Germany during that period. A marked improvement in food supplies produced a rapid fall in the mortality due to this infection. There can be no doubt that the previous state of nutrition may be of great importance in determining the result of an infection. In metabolic disorders such as those which result from disease of the pancreas, infection may also be a serious problem. In severely malnourished patients the tissues have an impaired ability to withstand toxæmia. Davidson, Meiklejohn and Passmore (1959) point out that one acute episode of infection in an infant weaned on a diet that is barely adequate is often fatal. Whenever the breadwinner is struck down by a prolonged infection such as tuberculosis, leprosy, relapsing

fever or yaws, nutritional failure is likely to affect his dependants who rely on his agriculture.

The relationship between diet and susceptibility to infection would therefore seem to be real and worth attempting to define in terms of greater precision than can yet be used.

THE INFLUENCE OF PROTEIN INTAKE

Dubos and Schaedler (1959) point to the divergences in the conclusions reached by different groups of workers concerning the influence of protein intake on susceptibility to various pathogenic agents. In this respect protein deficiency seems to be of particular regard, as observed in kwashiorkor and the exudative type of tuberculosis. Even transient nutritional disturbances, particularly those of protein level, may profoundly alter the resistance of animals to infection. According to Dubos and Schaedler, the proper balance of amino-acids is even more important than their total amount in determining resistance to infection. It is, of course, untenable in theory and unrealistic in practice to treat the metabolism of one nutrient, protein—or the effects of its deficiency—as if they occurred in isolation, uninfluenced by other nutrients. Deficiency states in man tend to be multiple. Diets that are low in protein are often low in vitamins, particularly of the B complex, and also in minerals such as potassium.

Hegsted (1959), reviewing some of the epidemiological data in relation to protein intake and disease, found that there is, on the whole, very little evidence of protein deficiency in adult man anywhere, including areas where diets are almost entirely of vegetable origin, and he cites the observations of Patwardhan (1955) in India. In Africa, Walker (1958) has shown that many vegetable diets appear capable of supporting the increased protein needs of lactation. Without denying that œdema can be produced by protein deficiency, the specific role of protein in hunger œdema remains obscure and caloric deficiency seems by far to be the primary determinant. Whilst most investigators hold that kwashiorkor, the disease of the 'unwanted one', is primarily 'protein undernutrition', and this would appear to be a correct description in areas where the protein content of the main carbohydrate foods (e.g. sugar, cassava) is very low, nevertheless, in other areas, this description possibly oversimplifies the situation, for several investigators have failed to identify the role of protein in the etiology of this condition. According to Waterlow (1959), for instance, the evidence is largely circumstantial, whilst Scrimshaw (1959) considers that there is strong epidemiological evidence to suggest that infection constitutes the most common precipitating stress. Whilst a protein deficiency will automatically limit the calorie intake, so starting the familiar vicious cycle, calorie lack may be more important in relation to physical status than protein lack. The high correlation between protein and calorie intakes is often ignored.

PROTEIN METABOLISM AND FEVER

The rapid nutritional deterioration which so often follows acute infections is often dramatic. It was about 75 years ago that the systematic investigation of this problem began with a few measurements on nitrogen excretion by patients with typhoid fever, and it was about 50 years ago that Coleman, Shaffer and DuBois began their classical studies of metabolic changes in patients with acute and chronic febrile conditions. The loss of nitrogen, sulphur, phosphorus and potassium following traumatic injury is somewhat analagous (Cuthbertson, 1959). The question arises as to how such changes affect the clinical course of the infection or injury and whether attempts should be made to modify them. In this respect we know considerably more about the effects of injury than of acute infections. Coleman and his co-workers and others found an increase in total heat production and protein destruction during the febrile period, but the increase in total metabolism was comparatively slight. During periods of great toxæmia the average increase was some 23 to 44 per cent. All the evidence from direct and indirect calorimetry showed that patients who are in the early stages of fever and who are on low diets rapidly approach the condition of starvation, having practically exhausted their stores of glycogen. The patients who are well fed seem to differ in no way from normal, but they must be given more food than normal to bring the quotients to the same level. Depleted glycogen stores are rapidly replenished during convalescence, the respiratory quotients rise to 'an extraordinary level' and the metabolism which has been on a protein-fat basis in fever appears then to be on a protein-carbohydrate basis.

Although fever probably plays a role in the elevated metabolic rate of the severely burned patient, Cope and his colleagues (1953) observed that the temperature rises in the patients were irregular and did not correlate with the metabolic rate. The increase in heat production after injury we have found to have its origin in increased protein catabolism, and not in increased fat and carbohydrate catabolism (Cairnie, *et al.*, 1957). Linser and Schmid (1904) had earlier concluded that in toxic fevers, when the temperature is above 39°C., any increase of protein metabolism must be due to the toxic processes and not to the hyperthermia. This may be the origin of the term 'toxic destruction of protein' which appeared so commonly in the earlier medical literature. Further evidence was obtained by dietary experiments and indicated that the 'protein destruction' found in patients with acute febrile diseases was not the result of the fever alone. Carbohydrate added to the normal diet prevented the increase in urinary nitrogen excretion by normal subjects whose temperature was raised by exposure to heat, but it had less effect in patients with typhoid fever or paratyphoid fever.

Shaffer and Coleman (1909) and Coleman and DuBois (1915) also found that considerably more food calories than their measured heat production had to be given to patients febrile with typhoid fever in order to achieve nitrogen equilibrium. More recently, Grossman and his associates (1945) found that negative balances

persisted in patients with meningococcal meningitis after the temperature had become normal and symptoms and signs of the disease had been abolished by drug therapy.

These workers have also pointed out that it is the 'gravity' of the acute infection which determines the intensity and duration of the metabolic response.

The experiments of Watkin and Steinfeld (1957) on patients with neoplastic disease suggest that where there is progressive protein depletion there is diminished resistance to bacterial and fungal infection and to physical trauma.

WOUND INFECTION

The problem of wound infection is inextricably bound to the problem of wound healing: impaired healing increases the probability of infection; conversely, infection delays healing. The experiments of Frank, Fine and Pillemer (1955) and of Sanford and Evans (1957) indicate that animals have a lowered resistance to certain bacterial infections in the early period after severe injury, particularly if shock is present or has occurred. Bacterial contamination, tissue necrosis, blood supply and the adequacy of surgical care are generally of overriding importance.

PROTEIN AND SUSCEPTIBILITY TO SPECIFIC EXPERIMENTAL INFECTIONS

In the experiments of Dubos (1955a, b) and Dubos and Schaedler (1957) profound differences in susceptibility could be elicited by changes in the dietary regimen, even when the latter did not affect the weight curves of non-infected animals. For example, mice fed on commercial pellets (which are adequate for growth) were much more susceptible to staphylococci than were mice receiving a 20 per cent. casein diet. A great increase in susceptibility to infections with *Staphylococcus aureus*, *Mycobacterium tuberculosis* and *Mycobacterium fortuitum* occurred when the protein was reduced to 9 per cent. casein even though the uninfected animals grew just as well on the latter diet. When the complete diet was replaced by one containing gelatin—which is deficient in certain essential amino-acids—as sole source of protein, the increased susceptibility took place within two days and normal resistance could be restored rapidly by adding casein in proper amount. Poor diets seemed to exert their resistance-depressing effects by interfering with the clearing power of the organs or by favouring the multiplication of the pathogens, at least during the first few days after infection. Preliminary indications were that the fat content of the diet was of great importance in determining the response of mice to experimental tuberculosis, but not to staphylococcal infections.

PROTEIN AND ANTIBODY PRODUCTION

Resistance to infection has specifically been related to protein nutrition, especially by Cannon (1945) and his colleagues in Chicago. They have

repeatedly shown a diminished agglutination titre under experimental conditions, using low-protein diets and plasmapheresis after immunization with many antigens in protein-deficient rats. Metcoff and his colleagues (1948), however, were unable to find a definite relationship between protein nutrition and antibody production. Post-war studies in Germany, although demonstrating the superiority of antibody production by well-nourished over under-nourished hospital patients and prisoners, led Gill to conclude that the differences were not of practical significance. Kühnau (1955) suggests that the ideal management of infection calls for a high-protein intake with antibiotics administered to prevent the effective utilization of dietary protein by the invading organisms. Judicious use of antibiotics and antipyretic agents is more capable of influencing the state of the disease than is the actual protein intake. The nutritional care of the patient is but a part of his comprehensive treatment.

EFFECT OF DIETARY FACTORS ON TISSUE RESPONSE

Smith and Dubos (1956) present the view that natural and acquired resistance depends more often upon the ability of the inflammatory response to create in and around the lesion a micro-environment inimical to the infective agent. It is likely, in their view, that disturbances in the general state of health often bring about qualitative and quantitative changes in the biochemical characteristics of the inflammatory area. These in turn may interfere with the processes which control the activities of micro-organisms within the lesion. As a result, the response of the body to infection, and consequently the micro-environment in which the infection process follows its course, are under the control of factors which may be metabolic or psychic in origin. This concept, according to Dubos, accounts in part for the fact that susceptibility to infection can change independently of the immunological state of the infected individual. Since changes in susceptibility can occur rapidly, and be extremely transient, the intensity of exposure to an infectious agent may be less decisive than the physiological state of the exposed individual in determining whether infection fails to take hold, becomes established, runs an abortive course, or evolves into overt disease.

There is no clear-cut evidence that the resistance to infection of the seriously injured patient is decreased but specific antibiotic or chemotherapeutic treatment is clearly of paramount importance in the treatment of infection.

The relation of nutrition to infection is thus not simple. As Schneider (1955) pointed out several years ago, when striving for abundance of food, we at the same time fail to recognize that in viral disease it is the well-nourished host which has minimum susceptibility. Geneticists have clearly shown that it is possible to assemble into one and the same host susceptibility to one disease and resistance to a second. Schneider suggests that specific nutrients must be examined in relation to specific infections. Nutrition falls below procedures such as vaccination, chemotherapy and antibiosis in a

hierarchial order. But the benefits which may arise from appropriate nutritional treatment of a patient with an acute infectious disease have been pointed out by DuBois. There is no need to be afraid that by giving of food the fever may be increased. In the past, on the old-fashioned semi-starvation diet of broths, lemonade, with egg white and milk in limited quantities, the typhoid state with emaciation, delirium, and tremors, was typhoid plus inanition. With the current liberal diets of 2000 or more calories a day there is but little emaciation or delirium.

SUBACUTE AND CHRONIC INFECTIONS

It has been inferred that subacute bacterial infections generally, including tuberculosis, lead to nitrogen wasting and/or depressed nitrogen storage. Statistical evidence relating the prevalence to poor socio-economic conditions, including poor nutrition, is well-known, and often there is an anorexia which accompanies the disease and which may complete a vicious cycle that is so evident. The total energy metabolism in tuberculosis tends to be proportional to the temperature. McCann (1922) reported nitrogen retention in tuberculous patients when they received from 70 to 140 per cent. more calories than their estimated post-absorptive basal expenditure and from 0.7 to 2.9 g. protein/kg./day. According to Levenson and Watkin (1959), the overwhelming clinical evidence, especially that obtained during the 1939-45 War, points to caloric undernutrition with or without qualitative dietary deficiency as the most common factor associated with an unfavourable course of the disease.

THE 'ANTI-INFECTIOUS' VITAMINS AND OTHER FACTORS

Any dietary deficiency which vitiates the health of the skin and mucous membranes and their secretions may be expected to increase the liability to infection. Certain other dietary factors, and in particular vitamins A and C, have long been claimed to protect the body against infection. Whilst there is no scientific evidence that resistance can be increased by intake of any one of the known vitamins above the level for a normal state of sound nutrition, it has been shown that certain dietary constituents can exert a protective effect against a few pathogens under conditions in which these constituents do not promote growth. A curious illustration of this is the increase in resistance to pneumococci and staphylococci exerted by cobalt in mice receiving excessive amounts of manganese in their diet (Hitchings, Falco and Sherwood, 1949). Boyden and Andersen (1955, 1956) have found that the resistance of guinea-pigs to tuberculosis in springtime is attributable to substances in their greenstuff other than vitamin C and other known nutrients.

There is no doubt that deficiency of vitamin A can lead to changes in the epithelial tissues, in particular the eyes, respiratory and gastro-intestinal tracts, which then render them susceptible to infection. Into the same category comes the gingivitis caused by vitamin C deficiency. Infection is

secondary. The frequent association of kwashiorkor and xerophthalmia in certain parts of the world has been reported. More recently it has been found that pseudo-tuberculosis, referable to *Corynebacterium muris*, often with a fatal outcome, may also appear spontaneously in animals maintained on pantothenate-deficient diets (Seronde, 1954; Zucker and Zucker, 1954). Thus famine can indirectly pave the way for pestilence.

But resistance can also be decreased by the addition of certain foodstuffs.

Thus, enrichment of the diet with seed oils, and particularly with wheat germ oil, aggravates mouse salmonellosis and tuberculosis (Dubos and Schaedler, 1959; Schneider, 1951). More striking still is the fact that nutritional deficiencies can increase resistance to infection. For example, riboflavine deficiency in chicks decreases the severity of infection by *Plasmodium lophuræ* (Seeler and Ott, 1946) and ascorbic deficiency in monkeys represses the multiplication of *Plasmodium knowlesi* (McKee and Geiman, 1946). So long as monkeys and rats are fed on a diet lacking in para-aminobenzoic acid they do not develop malaria because this vitamin is required for the multiplication of the plasmodium (Hawking, 1954).

Viruses in tissue cultures remain dormant as long as the infected cells are maintained in deficient culture media (Bader and Morgan, 1958; Heggie and Morgan, 1956; Johnson and Morgan, 1956; Morgan, 1956; Morgan and Bader, 1957).

Limitation of various vitamins and amino-acids retards the progress and changes altogether the character of several viral infections (Foster *et al.*, 1944; Haas, Briggs and Stewart, 1957; Leftwich and Mirick, 1949; Rasmussen *et al.*, 1944; Sprunt, 1942; Sprunt and Flanigan, 1956). The infected cells are prevented from carrying out the synthetic processes needed for viral replication.

Here we may have an explanation of the clinical experience that virus diseases often exhibit a less acute character in patients who are underfed or less well nourished. At this stage of our knowledge, however, it would be unwise to advocate malnutrition as a prophylactic agent against virus infections. Rather one would emphasize, with Howie (1949), that the nutritional state will not necessarily have the same influence on all infections. In mice the breakdown in resistance caused by nutritional deficiencies is rapidly reversible (Dubos and Schaedler, 1958; Schaedler and Dubos, 1956). This may account for the rapid recovery often noted among convalescing tuberculous ex-prisoners of war whose disease had become acute in prison camp.

The unique presence of *L. bifidus* in the intestinal flora of breast-fed infants has stimulated research on the nutritive requirements of this organism (György, Norris and Rose, 1954).

Strepogenin-like constituents of both human and cow's milk (György and Rose, 1955) and an additional enhancing factor, apparently specific for human milk (György, 1957), may act as supplementary growth factors, at least for the specific mutant of *L. bifidus*, namely *var. Pennsylvanicus*.

The role of *L. bifidus* in the physiology of the breast-fed infant is still shrouded in mystery, and not all would be prepared to go as far as Walch (1956) in suggesting that this organism is responsible for conferring immunity against certain enteric infections. This flora of the normal breast-fed infant is the pre-eminent example of a fermentative, saccharolytic, acid-

producing intestinal flora. The mixed flora of infants fed on cow's milk, as well as the intestinal flora at all other ages, is characterized by a multitude of various fermentative and putrefying aerobic and anaerobic bacterial strains, with the prevalence of putrefaction.

In 1949, Sears, Brownlee and Uchiyama recorded that the *Escherichia coli* flora of the intestinal tract of man at any one time consists usually of one or two strains which persist over long periods, together with a small number of other strains whose tenure is limited to a few days, a few weeks, or a few months. The long-tenure strains they designated as residents, the small number of other strains whose tenure is limited to days or months were designated as transients. Further observations (Sears and Brownlee, 1952) demonstrated that this pattern of bowel *E. coli* may be shown by very young babies as well as by adults, resident strains becoming established as early as ten days after birth. Diarrhœic attacks of short duration do not by themselves usually bring about changes in the resident strains.

These findings, taken in conjunction with the modern concept of the importance of the pattern of the normal bacterial flora in the body economy, might suggest that the lactobacillary flora of the breast-fed infant is of intrinsic value. But it might well be argued that it would synthesize very different nutrients from those synthesized by the heterogeneous intestinal flora of the artificially fed baby. The flora of the breast-fed infant consists of over 90 per cent. of gram-positive bacilli, whereas that of the infant on cow's milk is variable. The feeding of brands of 'adapted' milk have failed to produce stools with an acidity and bacterial flora similar to those of breast-fed infants.

BACTERIAL DESTRUCTION OF VITAMINS

Intestinal bacteria may also destroy essential nutrients; for example, vitamin C is destroyed *in vitro* by *E. coli* in the absence of more readily fermentable carbohydrate, whilst it is known that certain scorbutic patients will respond to injected but not to oral vitamin C (Young, 1942; Young and James, 1942; Young and Rettger, 1943).

Girdwood and Doig (1957) have shown that an altered flora may occur in blind loops or sacs of the intestine, and in intestinal diverticula. Halsted, Lewis and Gasster (1956) have reported that the anæmia in the 'blind loop' syndrome is unaffected by neomycin, which is not readily absorbed, whereas it may be cured by chlortetracycline, which is readily absorbed and may therefore appear in sufficient concentration in the 'blind loop'. Card (1959) points out that if there exists, under certain conditions in the intestine, an altered flora such that essential trace food factors are lost to the host, then the purely descriptive name of 'blind loop' should be abandoned and replaced by some name which describes the functional state of privation. He asks if we dare regard the fatty liver, which proceeds to fibrosis, seen in some patients with severe ulcerative colitis as, in part, a nutritional disease of the liver due to involvement of the cæcum and ascending colon: that is, that part of the gut which is said to be the main site of vitamin synthesis. It is probable, he points out, that the supplanting in man of bacteria which normally synthesize vitamins in the intestine, or the growth of bacteria

which themselves utilize substances required by the host, might result in a deficiency state.

ANTIBIOTICS AND NUTRITION

Since the intestinal flora has been shown to synthesize vitamins, it is natural to inquire into the effect of antibiotics on vitamin synthesis. In human subjects, only a few observations on the action of antibiotics in hastening growth have been carried out. The most impressive positive results with antibiotics on growth of children are those reported by Scrimshaw and Guzmán (1953) and Scrimshaw, Guzmán and Tandon (1954), on Mayan children 7 to 12 years of age living in the Guatemalan Highlands and subsisting on diets low in animal protein. A pronounced growth effect followed the administration of chlortetracycline. The response with penicillin was variable. A slight but definite effect of chlortetracycline upon the rate of weight increase, but not on the rate of height increase, was observed in a study on schoolchildren in Jamaica with a mild degree of malnutrition (Mackay *et al.*, 1956). The position has been admirably summed up by Coates and Kon (1955):

> 'It is generally accepted that antibiotics have a direct effect on certain metabolic processes, hence it is conceivable that, given in the diet, they exert a small but definite pharmacological action which contributes to their beneficial effect on growth, but that in ordinary environmental conditions such an action may pass unnoticed because of the overriding predominance of the bacteriological effect'.

CONCLUSION

The ability to confer or alter resistance to infection through dietary means is a property much more complex than is usually considered by nutritionists but is well worth attempting to understand and define in terms of greater precision. For this they must link up with the bacteriologists, protozoologists and virologists.

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NUTRITION AND OLD AGE

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It is the general belief that calorie requirements diminish as a person grows older. An early recommendation of the Food and Agriculture Organization suggested that a diminution of the calorie allowance of 7 per cent. for each decade after 25 years of age should provide the basis for calculating the calorie requirements of different age-groups over this age. A later report (F.A.O., 1957) recommended a reduction of 3 per cent. in the requirements for age 25 years for each of the decades 25 to 35 years, and 35 to 45 years, a reduction of 7.5 per cent. for the decades 45 to 55 and 55 to 65 years, and a further 10 per cent. reduction for the decade 65 to 75 years: in other words, a reduction of 31 per cent., or approximately one-third, for a person between the ages of 65 to 75. The same report also states that 'present knowledge of the influence of ageing on the quality of food eaten and energy expenditure is deficient and further investigations are needed'. The calorie requirements for the elderly, as for any age-group, will be determined by the composition of the body, the muscle mass, and the energy expended. Today the energy expenditure varies little between the ages of 30 and 60 but after 60 increasing infirmity leads to a diminishing demand of calories for energy purposes.

SOME SURVEYS

Pyke and his colleagues (1947) compared the diets eaten by old women living at home, old women living in almshouses, old people living in a large institution and old men living in a small institution. The calorie value of the diet was estimated from a daily diary of the food eaten. The calorie intake varied from 472 to 2,313 cal./day for the old women living at home, 1,079 to 1,877 cal./day for the old women living in almshouses and 1,251 to 1,717 cal./day for those living in a large institution. The ages, with two exceptions, ranged from 60 to 85 years. These values are below those recommended by F.A.O. and by the United States National Research Council. Jahnke (1961), on the other hand, in a nutritional survey in Germany among the over 70's, found an average calorie intake for the men of 2,300 cal./day and for the women of 1,900 cal./day which are much nearer the values suggested by F.A.O., but he found considerable individual variation, largely due to the variation in the degree of physical activity.

Bransby and Osborne (1953) in the Sheffield Survey found that the mean intake for men aged 65 to 75 was about 2,100 cal./day and for women of the same age-group 1,700 to 1,800 cal./day. These findings are in contradistinction to those of the National Food Survey reported by Baines and Hollingsworth (1955) which quotes values of 2,900 cal./day for women of mean age 60. What are the reasons for this degree of undernourishment

among the elderly? In their social survey at York, Rowntree and Lavers (1951) found poverty to occur in two groups: the elderly, and married men with a family of more than two children who had been unemployed for six months or more on account of ill health.

The returns of the National Assistance Board are also informative: approximately two-thirds of all those applying for supplementary grants in 1958 were old-age pensioners and nearly one-half of those applying for discretionary payments received a payment towards the cost of extra nourishment. Ill health, whether physical or mental, inability to shop, to move about the house, and to cook, fear of falling, loss of a partner, loneliness, lack of interest in preparing meals for one, difficulty in mastication are all contributory factors, as well as lack of financial resources, for elderly persons having an inadequate diet. It will thus be seen that a full medico-social investigation is vitally important if the majority of the elderly are to have an adequate diet in so far as calories are concerned.

QUALITY AND COMPOSITION

The whole basis of a sound nutritional policy for the elderly is not merely the provision of adequate calories. What is equally important is the quality and composition of the diet. When calories are deficient there is, of course, greater chance of finding other deficiencies. A careful analysis of the admissions to hospital in Great Britain has shown that only a small proportion of elderly patients are admitted on account of under- or mal-nutrition. Some cases may be missed because young doctors are unfamiliar with the conditions, and usually there is an associated element of general ill health or social factors which have contributed greatly to the development of mal-nutrition. Pyke and his colleagues (1947), in their survey, found evidence of inadequate protein intake, especially amongst elderly women and a deficiency also in the amounts of vitamins A, C, and D. A survey of the diets consumed by diabetic patients (Tunbridge, 1953) also revealed inadequate protein intake among the elderly patients. Osteoporosis is a common finding in the elderly, particularly amongst elderly women. Albright (Albright and Reifenstein, 1948) distinguished between osteoporosis and osteomalacia, but Nordin (1961) has suggested that there is no real difference and that the primary defect is one of inadequate calcium intake.

The lack of extensive metabolic balance studies in the elderly, particularly studies carried out over several years, makes it difficult to give a lead as to the minimal requirements for elderly subjects. Durnin (1956) is undertaking such studies in Glasgow and it is to be hoped that more reliable information will be obtainable in the near future. The position concerning minimal requirements is complicated by other factors. It is known that some elderly subjects have a diminished gastric, intestinal, and pancreatic secretion, that there is a decrease in renal tissue and an alteration in the amount of hormones secreted by the endocrine glands. All these factors may influence considerably the requirements of any given individual. The finding of low

values for vitamin B_{12} among the elderly, as also other components of the B complex, raises the question as to whether these are true deficiencies, or secondary deficiencies due to malabsorption, or whether they indicate lessened requirements. The increasing incidence with the passing of the years of diverticulosis and the secondary effects of the continuous use of purgation and other drugs on intestinal function are also factors influencing nutrition. By contrast, McCance and Widdowson (1955) reported that six starving old men responded just as well as six starving young men to a high-calorie diet suggesting that there was no basic defect in the essential metabolic reactions.

The inadequate knowledge of nutritional principles by the public, and lack of finance, often combined with frailty and ill health, are the main reasons for the occurrence of malnutrition or subnutrition among the elderly in Great Britain today. The protein and calcium deficiency might well be met by the national adoption of the policy used by McCay (1952) in dealing with the same problem in the Mental Hospitals in New York State: he added skimmed dried milk powder to the bread and was thus able to ensure an adequate diet without the need to change the feeding habits of the community.

DIET AND LONGEVITY

So far reference has been made to the inadequacy of the diet of the elderly because it is well recognized that undernutrition predisposes to disease and is often associated with a lowered resistance to infection. It is often asked whether diet can have a positive influence by increasing health or by increasing the duration of life. There is always the tendency for people to feel that if a little of something would do them good a lot would make them very much better. This is a dangerous doctrine in nutrition and considerable harm has been done to children through the adoption of this policy in relation to vitamin D.

Most of the experimental work concerning the possible beneficial effects of diet has been carried out in animals. McCay succeeded in retarding growth and prolonging the life of rats underfed from the time of weaning. No such result was obtained when dieting was started after the onset of puberty. The reason for the longevity was the slower development of the chronic diseases, affecting the lungs, kidney and middle ear which are the common causes of death in elderly rats. McCarrison found that the feeding of rats on diets corresponding to those of different races was followed by the development in the rats of a morbidity pattern of illness similar to those observed in the human races. Metchnikoff stressed the importance of intestinal flora and although not successful in prolonging his own life, the idea behind this theory is receiving much attention today. Alteration in the bacterial flora can have a profound effect on the growth of animals.

The major cause of death in the second half of life in the western world is cardiovascular disease. Malmros (1950) reported a fall in the death rate

from cardiovascular disease in the 1939-45 War in certain countries where there had been a fall in the consumption of dairy products and eggs. Since this report much epidemiological data has been collected which would suggest a relationship between fat intake, blood cholesterol levels and ischæmic heart disease. Later work has suggested that it may be the proportion of essential fatty acids which is the important factor. The present position is well reviewed by Bronte-Stewart (1961) but much more factual information is required before universal action can be taken, as any dietary alteration necessary to meet this point would require a radical reorientation of animal husbandry, food processing and preservation as well as a fundamental change in the feeding habits of the community.

CONCLUSION

It is difficult to formulate rules for the nutrition of the elderly. Certainly excess calories are to be avoided for many are the ills of obesity. Henry IV aptly remarked: 'One of them is fat and grows old, God help the while'. Heupke (1961) studied the habits of 30 men and women centenarians. Their diet was simple and consisted of bread, meat, abundant milk and yogurt, plentiful vegetables and fruit. Perhaps one cannot do better than to quote the advice of Thomas Cogan in the 'Haven of Health', 1596:—

'Consequently to preserve life is to use meates and drinks according to the age of the person for the dyet of youth is not convenient to old age nor contrariwise'.

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MALNUTRITION IN THE TROPICS

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MALNUTRITION in the tropics does not differ from malnutrition in temperate climes. Wherever it occurs it is due either to lack of food as a whole with a low calorie intake, resulting in marasmic conditions, or to lack of certain nutrients, giving an imbalanced diet, or to a combination of these two factors. The difference between tropical and non-tropical conditions lies in the presence of added stresses in the tropics. Population pressure and resulting poverty, poor hygiene, infections, especially tropical diseases such as malaria, infestation with worms which interferes with absorption of food from the bowel and, in the case of hookworm, anæmia from loss of blood, are all common in the less well-developed parts of the tropical and sub-tropical world. As well as these objective causes many more subtle factors are at work, such as ignorance of what are the best foods available, and customs preventing their use. The pregnant and lactating woman and the young child, being the more vulnerable groups, and being more affected by customs and superstitions, suffer most from these added strains. Similar results occur during times of war and it was during the 1939-45 War in prison camps in both tropical and temperate climes that advances in our knowledge of malnutrition, known to be the direct result of specific dietary deficiencies, were made.

It is thus evident that to a great extent malnutrition should be preventable, but most countries find prevention difficult and costly to achieve. Services for mother and child care have reached various stages of efficiency in different parts of the world but the tropical, less economically developed, countries still lag far behind the West in spite of all the United Nations agencies—the World Health Organization, the Food and Agriculture Organization and the International Children's Fund—have done to improve the lot of mother and child.

HISTORY

The background of malnutrition in the tropics is closely linked with the historical background of medical progress, and an understanding of this helps greatly in solving the problems as they occur today. Fifty years ago doctors were much concerned with the treatment of specific disease. This followed the acceptance of Pasteur's work, which proved that microbial agents caused disease. In the tropics practitioners were fully occupied with the treatment of such conditions as yaws, malaria, amœbic dysentery, and so on. Just after the 1914-18 War vitamins came into prominence and thus started the swing of the pendulum away from the exclusive ideas of Pasteur. Scurvy, pellagra, beri-beri were spectacular diseases with dramatic cures and doctors became almost obsessed with the benefits that vitamins could

bestow. People then began to realize that, although classical deficiencies were not common, the nutrition of the people in many parts of the world was clearly not satisfactory. Descriptions of nutritional disease kept cropping up from many places, but there was little coordination and most of the work was done in comparative isolation. Each observer used his own local name.

One of these observers was Ciceley Williams (1933), who observed and described children in West Africa with a disease which she called kwashiorkor: the disease of the displaced child, the child who becomes ill when the new baby is born and he is displaced from his only satisfactory source of food, the breast. This disease has come to be accepted as the most important cause of ill health and death among children in the tropics. Many people disagreed with Dr. Williams and said that the condition was not a new one, that it had been described years before, and that it was pellagra. This disagreement went on until 1945 and after, but Dr. Williams was adamant: kwashiorkor was a new disease, it was malnutrition, and it was not pellagra. She gave her reasons in detail (Williams, 1935).

But there was a setback to an understanding of kwashiorkor. In her early descriptions the presence of a rash was considered necessary for the diagnosis and for some time Dr. Williams, who by then was working in Malaya, did not find this rash in children suffering from a very similar disease of malnutrition. By 1954 completely typical cases had been found, corresponding to those originally described by Dr. Williams. The argument was finally settled when nicotinic acid became available for trial. Pellagra and its rash were cured by nicotinic acid, but kwashiorkor was not. Kwashiorkor was not pellagra.

After the 1939-45 War the work of observers all over the world—Europe, Africa, Asia and Tropical America—was sorted out and it was internationally accepted that kwashiorkor is a deficiency disease due to a diet deficient in protein. It affects typically the small child weaned from the breast and not yet able to cope with an adult diet, and it is mainly found in the less well-developed countries. Numerically the problem is a serious one and it is likely that nearly half the children in the 2- to 5-year age-group are affected.

In many countries an even higher proportion of young children show signs pointing to a deficient diet. So long as malnutrition among children is common, infections of all kinds will remain a serious menace to life (Scrimshaw, 1959; Scrimshaw *et al.*, 1960). The mortality among young children is high in all less-developed countries: in Malaya, for example, nearly half the total deaths occur before the age of 5 years, and many countries show an even heavier child mortality. The situation was well put by Bengoa *et al.* (1959):—

'Since the child below one year is usually protected by the mother's milk, and since the school-age child can compete at home for more and better food, the impact of protein-calorie malnutrition is specially noticed in children between one and four years of age.

'It is true that in official certification of deaths, diarrhœa is the first and most important cause of mortality in children under five years of age but, as has been shown by Scrimshaw *et al.* (1957), a great proportion of deaths attributed to either diarrhœal diseases or parasitism are really due to severe malnutrition. And, even more important, most of the deaths would probably not have occurred if the children had been fed properly.

' From the point of view of vital statistics, it appears that the mortality rate in children one to four years of age may be a good indicator of the protein-calorie malnutrition problem in a given area or country.

'Bengoa in 1955 was of the opinion that when the mortality rate in the one- to

four-year age-group is more than 10 per thousand it could probably be related to a serious protein nutrition problem, although other factors would be contributing to this high mortality. There are still countries in which the mortality rate in children one to four years of age is above 30 per thousand, whereas in the United States of America, England, and North European countries it is about 1 or 2 per thousand'.

THE PROBLEM: A BALANCED DIET

In countries where a staple cereal forms the major part of the diet the total protein intake tends to be low, and the animal protein very low, resulting in an imbalanced diet. The B group of vitamins, especially aneurine and riboflavine, may or may not be low but it is likely that they will be below the recommended allowances for the different age- and sex-groups.

Many surveys have been done in different parts of the tropical world and, although there are variations from place to place, basically the shortages are the same in all less well-developed countries. There is one important difference: diets of the rice-eating countries of India and the Far East as distinct from maize-eating Africa are low also in vitamin A. In South and Central America, although maize is eaten to some extent, the vitamin A intake is low and xerophthalmia does occur, but it is not the serious problem that it is in the Far East (Autret and Behar, 1954; McLaren, 1958). Recommended dietary allowances have been worked out in various countries and the most recent are those of the Food and Nutrition Board of the United States National Research Council (1958).

Those wishing details of recommended allowances should study this booklet which is most informative and enables allowances to be worked out for any individual, with adjustments for climate, average weight, age and sex, including special allowances required during pregnancy and lactation, and for growth in babies of one month to the adolescent boy or girl.

In order to check the nutrient intake in a particular individual, or series of individuals, several methods have been devised making use of food tables in which details of the composition of foodstuffs are given. All food that is eaten over a period of time is weighed and from this the nutrient intake is calculated from the tables. If weighing is not done a twenty-four-hour recall of food eaten may be recorded. It has been found that in the case of simple diets methods of recall are likely to give results as accurate as by weighment (F.A.O., 1954; Padmavati *et al.*, 1958). It is by these methods of dietary investigation, together with biochemical estimations of body fluids, that, broadly speaking, certain clinical signs can now be associated with certain deficiencies in the diet. These investigations are far from complete and there have been some conflicting results in experimental work.

SPECIFIC NUTRITIONAL DISEASE

Certain specific conditions due to faulty nutrition must be mentioned, although these are well known and present no difficulty to the practitioner.

In order to give a guide to the reader a figure for the recommended allowance of the different nutrients has been bracketed beside the specific condition mentioned. It is no more than a guide and the figure chosen is that for a child of 1 to 3 years of age whose weight is around 12 kg. For temperature adjustment there must be a 5 per cent. reduction of calories for every 10°C. of temperature above the standard temperature (20°C.).

Rickets (Calcium 1 g. Vitamin D 400 I.U.).—Rickets does occur in the tropics and this is partly due to the low calcium intake. Deficiency of calcium is common in countries where little milk is available or where it is not an accepted food. Fats and fat-soluble vitamins are low in most tropical diets. That rickets is not more often seen is due to the presence of adequate sunlight. Sometimes, however, the child is too much protected from the sun in an endeavour to preserve the much prized fair complexion.

Beri-beri (Aneurine 0.6 mg.; 0.3 mg. for every 1000 calories. More is needed if carbohydrate is high).—Beri-beri is not uncommon in countries where highly milled rice is the staple diet. Aneurine tends to be low in all tropical diets but, where cooking methods involve the throwing out of excess water when rice is cooked, the shortage becomes a serious one. That the discarding of the aneurine-containing cooking water does seriously affect nutrition is seen in the contrast between India and Burma where this is done, and Malaya where in Chinese and Malay cooking all the water is absorbed by the cooked rice. Patients may be greatly helped with cooking hints on these lines, as it is not generally appreciated how much of the B vitamins and vitamin C are lost in the cooking water of vegetables. In Burma beri-beri is a serious problem and many infant deaths occur. In Malaya, although post-natal women are liable to show signs of vitamin B deficiency—some numbness and tingling of lower limbs or some greater degree of lower motor neurone paralysis—and it is known that breast milk is low in aneurine (Simpson and Chow, 1956), deaths from acute beri-beri are rare.

Scurvy (Ascorbic acid 35 mg.).—It is unusual to find scurvy in tropical countries. Unlike the more developed countries breast feeding, although regrettably on the decline, is still quite common and the child, as soon as he or she is able, has a taste for any jungle fruits that are available. Thus, although the vitamin C intake is low, it appears to be adequate. It is a strange comment on advance in the West that it is now the bottle-fed western baby who runs the risk of developing mild scurvy.

Pellagra (Nicotinic acid equivalents 8 mg.).—Pellagra is not a serious problem and in numerous tropical surveys the intake of nicotinic acid has been found to be adequate. It is now known that tryptophan, a precursor of nicotinic acid, is readily converted to nicotinic acid in the body and so when a dietary analysis is made both tryptophan and nicotinic acid must be included. (60 mg. of tryptophan are equivalent to 1 mg. of nicotinic acid.) The typical skin rash on exposed parts of the body, which become photo-sensitive, occurs as an early sign, and sometimes creates confusion with kwashiorkor in a child. Occasionally kwashiorkor and pellagra occur together. Pellagra is readily cured by giving nicotinic acid.

Night blindness, Bitot spots, xerophthalmia and keratomalacia (Vitamin A 2000 I.U. Protein 40 g. Calories 1,240).—Diets poor in fat and low in vitamin A and carotene, as are all diets in the Far East and in India, lead to serious eye disease. In Malaya nearly half the cases of blindness are due to keratomalacia (Thomson, 1953). There is some evidence that a low serum

protein contributes to the seriousness of low vitamin A and carotene intake, by interfering with the transport of such vitamin A as may be stored in the liver (McLaren, 1958; Bagchi *et al.*, 1959; Arroyave *et al.*, 1959; Friend *et al.*, 1960).

For the treatment of these conditions it is important to spread the knowledge of the early signs. Mothers soon learn to realize the importance of night blindness, and to report it to the doctor or nurse. Slight degrees of xerophthalmia, crinkling of the conjunctiva and early Bitot spots, are all danger signs and should be treated at once with parenteral vitamin A. Early cases will soon show improvement after one or two injections of 100,000 I.U., but it is important to stress the need for added protein and vitamin A in the diet. Where UNICEF aid is available skim milk is a satisfactory supplement for the poorer masses but better still is fish flour which in many countries is most acceptable. Fish flour is becoming available in a number of countries, and is likely to replace skim milk, especially where there is no local dairy industry and where fish products are familiar and popular. For better-off patients there are several high-protein products on the market made from milk solids with added vitamins and minerals.

Hyperkeratosis.—Hyperkeratosis or phrynoderma is not an uncommon skin condition in young children, and is a useful guide suggesting a deficiency of vitamin A in the diet.

Angular stomatitis (Riboflavine 1 mg.).—Angular stomatitis is often found in mothers, and also in children of both pre-school and school age. The cracks at the angles of the mouth may be slight and go unnoticed, or may be associated with a painful cracking of the lips and general stomatitis. It is likely that the lesions are due to a number of deficiencies, but they are readily cured by giving 5 mg. of riboflavine daily. Improvement in the diet as a whole is also important.

Anæmia (Iron 7 mg.).—Iron-deficiency anæmia is common in tropical countries. Mothers are often grossly anæmic and babies who are not given an iron supplement rapidly show low hæmoglobin levels. Much can be done by giving advice about diet but, when only little animal protein is taken, a supplement of iron is usually needed. Intramuscular iron, in spite of recent comment on risks associated with its use, is a useful preparation, particularly in countries where a pill or mixture tends to be left untouched after the first dose or two. Treatment with iron is important, as children of school age are still anæmic, and the girl of 12 or 13 years is soon likely to suffer to a more severe degree as the result of early childbearing.

KWASHIORKOR

(Protein 40 g. One-third to a half should be from an animal source to ensure the presence of all the essential amino-acids.)

As already noted, kwashiorkor occurs in many tropical and non-tropical countries and is primarily due to a lack of protein in the diet of the child who is being weaned from the breast (Williams, 1933, 1935; Brock and

Autret, 1952; Trowell *et al.*, 1954; Thomson, 1954, 1958, 1960). Associated multiple vitamin deficiencies often complicate the picture. While on the breast, even if the mother is malnourished, the child is likely to escape, although the condition may occur before one year of age. The typical age is 3 to 4 years, when the child is off breast milk but is not able to take an adequate adult diet. The idea of special dishes for a child of this age is almost unknown except for paps made from the staple cereal. The calorie intake of these children may not be low; indeed, those whose calorie intake has been high show the most severe signs. This is usually due to a disproportionately high carbohydrate intake. It is well known that the child on the breast alone until two years of age is in a better nutritional state than the one given excess of carbohydrate supplements.

The recognition of the early phase of kwashiorkor is all-important. The mother reports a lack of appetite. This, on questioning, is usually found to be a distaste for the staple food and not a true anorexia. If the child is given an appetizing protein-rich meal he will eat with avidity, but as the disease progresses a true loss of desire to eat develops. Diarrhœa may be troublesome and will have been noticed by the mother, who is likely to have made matters worse by still further restricting the child's protein intake. Doctors, too, must beware of this danger. The mother may also have noticed a change of temperament in the child: previously cheerful and happy, he is now miserable and peevish, later, as the disease progresses, becoming apathetic.

On examination the doctor will notice that the child is flabby, due to muscle wasting; a two-year-old may be unable to walk. There may be some dryness of the skin and the hair may be depigmented, dry, or sparse and brittle. A little later, œdema develops, first on the dorsum of the feet and, as the disease advances, becoming generalized, but without ascites. Muscle wasting is now masked by the œdema. On palpation of the abdomen an enlarged liver may be found—in some cases to the level of the umbilicus (Davies, 1948, 1951). The early dryness of the skin may develop into a widespread eruption. The flaky paint dermatosis is typical of the disease, and is made up of areas of pigmentation which crack and peel off, exposing depigmented and sometimes raw areas beneath. The distribution is quite unlike that of pellagra and occurs on any part of the body (Williams, 1935). Some or all of these signs may be present in the later stages of the disease, and the child is now desperately ill. Without treatment mortality is very high indeed. Even with expert hospital attention many die if they have been left untreated until the later stages of the disease. The early, less severe, stage may continue for many months, or it may be precipitated rapidly by some infection into the serious condition of acute kwashiorkor; diarrhœa, measles, pneumonia or other infections are likely to do this. There is a close connexion between infection and kwashiorkor (Scrimshaw, 1959; Scrimshaw *et al.*, 1960). A well-fed child might survive these infections but one suffering from protein-calorie starvation, a descriptive term used

to include the wider manifestations of kwashiorkor, is much less likely to do so (Jelliffe *et al.*, 1957).

One of the most serious complications is a vitamin A deficiency resulting in keratomalacia and blindness. This is a common complication in Indonesia (Oomen, 1953) and also occurs in other parts of the Far East.

Fatty degeneration of the liver is often found and it is likely that it is always present at some stage of the disease. In some cases the liver later becomes fibrotic, but the relationship between fat deposit and fibrosis is not fully understood. It is thought that degeneration of pancreatic cells precedes the liver changes, and the enzymes, lipase, amylase and trypsin, are reduced. In the plasma, total protein and albumin are low whilst globulins, notably gamma globulin, appear high. Blood urea and total cholesterol are low and also amylase, alkaline phosphatase and cholinesterase.

Early in the disease the doctor can help much with suggestions about diet and, if the child is one who attends a maternal and child health centre, advice will be given by the health visitor. At these clinics health visitors demonstrate simple dishes, such as a raw egg stirred into a plate of hot soft gruel, soup made from bones, and vegetables, both green and pulse types, with fish and meat added if the mother can afford them. Hints on shopping to the best advantage are also given. These remedies may sound unduly simple but ignorance and custom, as well as poverty, cause these feeding difficulties in most developing countries. The recognition of the early phase of the disease is all-important and, at this time, an improved diet with a high protein content will work a miracle of cure. At the same time infections and infestations must be dealt with. Antibiotics, the modern piperazine preparations for the treatment of ascariasis, and bephenium for hookworm, are a boon to the doctor who no longer need dread the use of toxic drugs. When the disease is both acute and severe, good nursing is essential. Suitable regimes have been worked out which include a high-protein diet supplemented with vitamins. Anyone interested in the details of treatment should refer to an article by Jelliffe and Dean (1959).

OTHER NUTRITIONAL DISEASES RESULTING IN LIVER DAMAGE

Indian childhood cirrhosis.—This type of liver fibrosis is common in India in the 1- to 4-year age-group (Jelliffe *et al.*, 1957; Robinson, 1958). It is not essentially a disease of poverty, most of the children belonging to well-off parents. The etiology is unknown although there are various theories: infective, toxic, nutritional and hereditary. The clinical picture is usually one of a well-nourished child between the ages of 1 and 4 years. The onset is insidious. The liver is enlarged and hard, and the spleen is palpable; late in the disease ascites develops, there is jaundice, and bile appears in the urine. There may be some fever. Plasma proteins are usually low, as they are in kwashiorkor, but skin changes do not occur. The prognosis is hopeless and, when clinical cirrhosis is established, it is only a matter of months before death occurs.

Veno-occlusive disease of the liver.—In Jamaica a disease of the liver in children has been described (Waterlow, 1948; Hill, 1951, 1955; Bras, 1955; Bras and Hill, 1956; Bras *et al.*, 1956; Waterlow *et al.*, 1956). The child is usually undernourished and between the ages of 1 and 5 years. The diet is low in protein, and 'bush teas' have often been given. Clinically the condition is similar to that of Indian childhood cirrhosis but with one important difference: veno-occlusive disease may present as an acute condition with hepatomegaly and ascites; this acute episode does not appear to occur in Indian childhood cirrhosis (Rhodes, 1952; Hill *et al.*, 1953). 'Bush teas' are made from a species of *Crotalaria* and *Senecio* (Schoental, 1957). At present it is thought that both a poor diet and the toxic alkaloids in the 'bush tea' contribute to the production of the disease. Treatment consists in a good diet rich in protein, and some children make a good recovery.

Vomiting sickness of Jamaica (*acute toxic hypoglycæmia*).—Vomiting sickness, associated with malnutrition and liver damage, is a toxic condition occurring in Jamaican children between the ages of 2 and 10 years. It is an acute illness with an onset of vomiting. Recovery may be complete, but often after an onset in which the child is drowsy he lapses into coma with convulsions soon followed by death. In some cases there may be no vomiting and the child rapidly goes into a fatal coma. The disease is thought to be due to the ingestion of the arillus of the ackee fruit (*Blighia sapida*): hypoglycæmia has been produced in laboratory animals by extracts from the fruit (Hassall and Reyle, 1955; Stuart *et al.*, 1955). Treatment consists in raising the blood sugar by intravenous dextrose, sedation for the convulsions, and an adequate protein diet.

PATHOLOGY OF LIVER DISEASE IN CHILDHOOD

The pathology of these four diseases in children which are associated with malnutrition and liver damage has been the subject of a great deal of discussion and argument in the past ten years. The final findings have not yet been reached. There is, however, some degree of agreement. Malnutrition is one of the factors producing the liver lesions, a shortage of protein in the diet being the main dietary deficiency. In kwashiorkor a fatty liver results. Some of these livers later become fibrotic, but the relationship between fat deposit and fibrosis is not fully understood. In veno-occlusive disease, and in Indian childhood cirrhosis, fibrosis is the main lesion. Children who die of vomiting sickness in Jamaica are likely to have accumulation of fat in the liver. The fact that 'bush teas' and the ackee fruit are almost certainly the toxic agents in these two latter diseases has spurred on those who feel that there may be other toxic agents at work, possibly in as yet undiscovered herbal remedies.

SUMMARY

Malnutrition in the tropics is a socio-economic as well as a medical problem. It does not differ from malnutrition in temperate climates but added stresses in the tropics make the problem a serious one.

The basic dietary deficiencies are those of protein and some vitamins. Calories may also be low.

Classical clinical vitamin deficiencies are not common, but there is much ill health due to imbalance of the diet, and infections which in a well-fed child would not be serious are likely to end fatally.

Often associated with a poor diet are toxic influences such as herbal remedies which are not yet fully investigated or understood.

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NUTRITION AND ATHLETICS

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EVER since men prepared themselves for athletic contests, the part played by diet has received an undue share of importance, credited with possibilities generally imaginary and always exaggerated. Foodstuffs were classified as good or bad for 'the wind', emphasis was laid on the virtues possessed by some, on the evils supposed to lurk in others. It was supposed that certain articles of diet contained principles that could increase respiratory depth, improve the force of the heart-beat or the vigour of the circulation. Manuals of training advised the high jumper to take 'food that confers agility' and the hammer thrower 'those things that make for strength and formation of blood'. (The recommendations ended at this stage, the selection of articles was left entirely to the reader.) One might as well suggest for the nightingale a diet that by some mysterious alchemy would be transmuted into melody, instead of the grubs, earwigs and field-lice selected by Nature.

A FUNDAMENTAL ERROR

Muscular strength, it was supposed, could be acquired by the ingestion of food, especially proteins. The chief part of training was—to use a current phrase—to pack in as much beef and mutton as possible and go on the river to row it into you, thus mistaking the order of natural requirement that exercise should regulate diet and not the reverse, for this unphysiological procedure was adopted independently of appetite and of the capacity to digest, absorb and assimilate. It is, of course, now realized that it is only by the work performed that a man's bodily strength or athleticism increases and that food contributes to the process of development only in so far as it provides a source of energy: there is no foundation for belief in specific properties of any individual constituent. That there is to some extent still a survival of the belief in the necessity for athletic hyperalimentation is indicated by the figures advanced by a German writer during the Olympic Games in Berlin in 1936.

The daily allowance included two large beefsteaks, two pints of milk (1 litre), half-a-dozen eggs; salads, sugar, honey, bread *ad lib.*; comprising three times as much protein, five times as much fat, one-and-a-half times the carbohydrate consumption of a man's habitual allowance, with the fantastic value of 7,300 calories. Yet the energy expenditure in athletic performances is comparatively slight, amounting to perhaps 600 calories in the Boat Race from Putney to Mortlake, and only 2,500 even in a Marathon race; and these are exceptional efforts.

At the same time one must avoid over-simplification by thinking of calories alone. For apart from the physiological element in ***nutrition***, there is the psychology of *eating* which is often a matter of habit, bearing no mathematical relation to the body's demand for nourishment. We eat not only to satisfy hunger but to gratify the palate and for other reasons, not excluding

that of passing the time. Consideration must be paid to the athlete in training excluded from many of life's amenities, and some generosity of dietetic provision is justified on a psychological basis. Long-distance road-racing cyclists are relatively abstemious, notwithstanding their large physical output. This is explained by their less emotional, more placid temperament compared with the more highly strung track athlete, and their independence of stimulation from eating as well as in other respects.

We understand some of the misconceptions of old-time trainers and athletes who in their anxiety to avoid the wrong path often strayed from the right. Observing that overcooking hardened the fibres of meat and rendered it indigestible, they went to the opposite extreme and ate it nearly raw. It seemed to them that everything palatable taxed the digestion, so that injunctions and prohibitions led to the creation of a monotonous, distasteful, even nauseating regime that invited staleness, boils and other minor illnesses, only too frequent in the past and not entirely absent today.

On the whole, experience and modern physiology have shown how small a part diet plays in athleticism. Certain traditions and fetishes that persist are relatively harmless and have the attraction of imparting a sense of mystery.

VEGETARIANISM

It is necessary to investigate this cult solely in relation to energy value. We may sympathize with sentimental, æsthetic, and hygienic aspects but they are not the present concern. Nor need we debate the various interpretations of the term itself, for, in practice, 'vegetarianism' means only the exclusion of flesh foods through which blood has circulated and, to obtain which, slaughter is required. Apart from this, a 'vegetarian' diet has an adequate caloric value, contains first-class animal protein, vitamins and other essentials well balanced in all respects. It remains only to inquire if there is any special virtue for athleticism in meat; in its proteins or other constituents. I am inclined to think there is, but proof would demand most exhaustive investigations. The 'he-man' is as a rule a hearty meat eater, but we are not entitled to assume that his prowess results from his partiality. It may be that he is the type that is attracted by meat, its sapidity, its satisfying property.

LIQUID

One of the outstanding principles of old-time training was that the least quantity of liquid should be permitted compatible with life; certainly far less than that compatible with comfort. Like other training misconceptions restriction had a logical explanation and persists, although the original necessity has long since disappeared.

Originally, feats of pugilism, pedestrianism, and oarsmanship were restricted to professionals, men of gross habits in whom preparation for a contest demanded drastic curtailment of their customary habits of gluttony and intemperance. When sporting contests became fashionable, the young bloods of the period, passing from the role of patron to that of active partici-

pant, copied the practices of their professional confrères, more especially since at that time comparison in matters of self-indulgence would hardly have been complimentary to the amateurs. Yet, although the original necessity has disappeared, the idea extended to liquid quâ liquid, every drop of which was presumed to be harmful, as conducing to weakness. And, although the evil of dehydration has by now been appreciated, there still persists a prejudice to a certain extent, especially in the case of professional boxers to whom no amount of argument seems to appeal.

A moderate indulgence in alcoholic beverages is generally accepted as helping to mitigate the rigours of training, but this is not to justify their deliberate employment as of special value. At one time, trainers *insisted* on two glasses of wine daily: sherry for the boxer and port for the oarsman (or perhaps it was the other way about).

SOME FADS AND FANCIES

The modern athlete is usually left alone with his dietetic likes and dislikes; it is appreciated that different machines work best on different types of fuel; any craving for a special foodstuff is accepted as a natural instinct and not, as in the past, reprobated and forbidden; Nature is accepted as a very efficient guide. Nowadays, as one might expect, attempts are made to justify certain articles for their vitamin content, but experiments have led to contradictory conclusions and it may be agreed that Nature, if not unerring, is a very efficient guide.

From time to time there is an ephemeral vogue for diets or foodstuffs of an unusual character. If a prominent athlete publicly attributes his success to his dietetic practice, especially if this is outstandingly bizarre, he will not lack for imitators who think they have only to follow his methods to achieve his success. The fallacy of deducing general principles from isolated examples is obvious.

Nearly half a century ago the Cambridge eight created a sensation by 'training on eggs'—ten or a dozen a day. A few years later, oranges were in the forefront. Shortly before the last War, an eminent physician attributed the continuous success of Light Blue crews to their indulgence in sugar. I wrote a facetious article describing how the cunning Cantabs had cornered all the famous Oxford marmalade, which, considering that I had some years previously been prominent in advocating the use of sugar in athletics, was probably rather reprehensible on my part.

The fact is that, whilst sugar is a valuable foodstuff for muscular exertion, there is no foundation for the belief that it can act as a sort of explosive capable of providing immediate energy, a claim sometimes advanced in the advertisements of enterprising manufacturers of glucose. It is true that cane sugar must, before absorption, be converted into the mono-saccharide, but the rapidity of hydrolysis hardly justifies a choice of glucose because of its superior speed in absorption.

A few athletes are convinced of the advantage of milk and indulge in several pints daily: surely an absurd addition to an already adequate diet. Any alleged advantage would be indistinguishable from the psychological factors in motivation or from the result of progressive training.

DIET AND ALLERGY

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THE relative vagueness of the term, allergy, and the injudicious attribution of allergic to a variety of conditions and disorders, whose etiology is still unsolved, as well as the lack of precise laboratory methods in establishing a diagnosis of allergy have created a curious state of affairs; so much so that the scientifically thinking physician will only reluctantly make such a diagnosis—almost as if he were ashamed of admitting to such dilettantism.

Seasonal respiratory allergies, such as hay fever and pollen asthma, have found general acceptance as have certain hypersensitivity reactions of the skin and gastro-intestinal mucosa to a variety of drugs and a few rarer foodstuffs. An allergic response to a number of basic foods such as cow's milk, cereals and eggs has been recognized to occur in infants and young children but seemed unlikely in the adult until more recent studies on ulcerative colitis brought this point into focus. There seems to be most convincing evidence that allergic manifestations may arise at any age after ingestion of a great variety of foodstuffs. If the disease is limited to the digestive tract the term, gastro-intestinal allergy, is used. If, however, foods are the allergens, but signs and symptoms arise in organ systems other than the gastro-intestinal tract, the description of alimentary allergy has been employed.

GASTRO-INTESTINAL ALLERGY

There are no pathognomonic manifestations, and symptoms attributable to an allergic reaction of the gastro-intestinal tract may also accompany a number of organic or functional disturbances. Nevertheless there emerges a certain pattern referable to the primary allergic response in the intestinal wall mediated by the release of such substances as histamine, acetylcholine, bradykinin, and 5-hydroxytryptamine: namely œdema, hyperæmia, smooth muscle spasm, abnormal mobility and excessive production of mucus.

COW'S MILK ALLERGY

Considerable attention has recently been paid to the occurrence of cow's milk allergy in infants. With the decrease in breast feeding and the corresponding increase in cow's milk feeding of young babies, a higher incidence of cow's milk allergy was bound to be observed. The frequency of the condition varies with the observer and the diagnostic criteria applied. Figures given have ranged from 0.3 per cent. (Collins-Williams, 1956) to 7 per cent. (Clein, 1954). In my own experience there were three cases in each 1000 consecutive hospital admissions under 1 year of age. The symptoms seen in all the patients were vomiting and diarrhœa; less common was their failure

to thrive and only in a third of the patients did actual weight loss occur. Colic was recorded in under 30 per cent. The diagnosis was mainly based on clinical evaluation of the history, a close correlation of the time of the onset of the gastro-intestinal disturbance with the introduction of cow's milk into the baby's diet, disappearance of the symptoms with elimination of milk and their reappearance with its addition. The elimination diet was only started when careful clinical and laboratory investigations had excluded any organic disorder. Demonstration of humoral antibodies although attempted was unsuccessful. The level of complement-fixing antibodies (Berger, 1958) as an index of allergic activity is sometimes helpful. Skin tests are generally negative and the search for eosinophil cells in the rectal mucus often unsuccessful. Besides the manifestations already mentioned, symptoms reminiscent of anaphylactic shock have been noticed in rare instances, as well as syndromes simulating cœliac disease.

Cow's milk allergy is a self-limiting disease and spontaneous recovery is likely—sometimes even after many months of ill health—unless severe infections complicate the issue during the period of malnutrition that may have arisen. The development of other forms of allergy at a later stage, in particular asthma, may indicate the correctness of the initial diagnosis. Hereditary factors, as suggested by a family history of allergic disorders, can only be regarded as evidence of minor significance. Until recently *alpha*-lactalbumin was regarded as the most antigenic of the milk protein fractions. Ratner and his co-workers (1958), however, have shown that *beta*-lactoglobulin is by far the most potent stimulus for antibody production whilst lactalbumin and casein, although more heat-stable, are less allergenic.

Management of a young child with cow's milk allergy presents certain problems, but the milk of a different animal species such as goat's milk or certain soybean preparations (of which 'wanderlac' is an example), or amino-acid mixtures, as represented in 'nutramigen', can be used successfully. 'Allergilac' is a powdered milk from which lactalbumin has been removed and therefore of benefit only in cases in which this particular fraction is the allergen. Its usefulness is thus limited. A formula which can be prepared in the home and has proved its value in the milk-free diet required for galactosæmic infants was published some years ago (Holzel, *et al.*, 1958). It is essential to remember that none of these substitutes replaces milk quite adequately even when vitamins and minerals are complemented. They should therefore be given for as short a time as possible and only after the diagnosis has been regarded as definitely established.

CŒLIAC DISEASE

The successful treatment of cœliac disease with gluten-free diets has raised the question of how this substance exerts its harmful effect on the absorptive capacity of the gut. The Dutch authors (Dicke, 1950; Weijers and Van de Kamer, 1959), who first recognized the injurious properties of the gluten-containing cereals, assumed a direct toxic action, whilst Berger

and Freudenberg (1959), on the basis of their studies of the antigenicity of gliadin, favour the concept of an allergic reaction to this gluten derivative.

EGG ALLERGY

Egg is a powerful antigen but the allergic response it evokes often manifests itself outside the gastro-intestinal tract and thus joins the group of disorders described as alimentary allergies. Vomiting, diarrhœa and colicky abdominal pain may follow its ingestion and on rare occasions these symptoms may be accompanied by enlargement of the liver and mild jaundice. Contrary to the findings in cow's milk hypersensitivity skin tests are often strongly positive. Elimination of egg from the diet is relatively easily carried out but it is equally important to exclude all the foods in the preparation of which it is an ingredient.

ULCERATIVE COLITIS

For nearly twenty years the opinion has been voiced that allergy to such foodstuffs as milk, eggs and cereals may play a part in the etiology of certain cases of ulcerative colitis (Andresen, 1942; Rowe, 1942), but this view found little acceptance until fairly recently when a number of authors from different countries have been able to substantiate the original observations (Sarles *et al.*, 1959; Rider *et al.*, 1960; Truelove, 1961).

The etiology of ulcerative colitis still remains obscure and no single factor so far can be incriminated in every case, but observations are accumulating lending support to the theory of food hypersensitivity as an explanation in some patients. Lagercrantz and his colleagues (1958), reviewing the extra-colonic manifestations in 48 children with chronic ulcerative colitis, came to the conclusion that the changes noticed in skin, joints, mouth and the vascular system, were due to hyperergic reactions.

Truelove (1961), in a study of five patients, found milk protein as the common sensitizing agent. Rider and his co-workers (1960), using an intramucosal test, which they developed, on 11 patients with ulcerative colitis obtained positive reactions in nine. Biopsies taken after twenty-four hours from the sites of the reactions showed acute vasculitis with a peri-vascular inflammatory cell infiltration containing large quantities of eosinophil cells. Four of the nine patients were hypersensitive to milk alone and one to egg alone whilst the others reacted to more than one foodstuff. All patients improved on a diet eliminating the allergens detected.

ALIMENTARY ALLERGY

The majority of cases of infantile eczema are the result of hypersensitivity reactions to ingested foods. Milk, milk products, egg and cereals are the most common antigens, but a variety of other foods may precipitate the dermatitis, such as fish, meat and fruits. The discovery of the allergen is not always followed by an improvement in the child's condition. The reason for this is to be found in the type of the skin lesion. A multiplicity of external factors of a physical or chemical nature may well prolong the inflammation even after the initial cause has been detected and eliminated.

In a number of patients the respiratory tract may provide the shock organ and a persistent brassy or barking cough may often be the reason for seeking medical advice. Asthma, although mostly due to inhaled allergens, can on occasion be initiated by hypersensitivity to certain foods; this is particularly so in the very young asthmatic under 2 years of age, by no means a rare event. Egg allergy in addition to the gastro-intestinal symptoms may induce angioneurotic œdema, which can also follow the ingestion of other foods. Anaphylactoid or Schönlein-Henoch's purpura often seen in the wake of a streptococcal throat infection is probably a hypersensitivity response to different antigenic stimuli, of which food can occasionally be one.

Urticaria, although allergy cannot be proved in every instance, is most commonly caused by foods, especially in childhood. A close time relationship between the ingestion of a particular food and the eruption of the urticaria is more helpful than diagnostic skin tests or the passive antibody transfer reactions. Migraine, varying in its etiology from case to case, has been claimed by allergists to fall into the realm of their specialty. A striking incidence of familial allergic disorder in such patients supports their contention and there is no doubt that occasionally it may be caused by a dietary antigen.

SUMMARY

A large number of foodstuffs can act as antigens inducing an allergic response in various tissues of the human body. The clinical manifestations may be limited to the digestive apparatus—gastro-intestinal allergy, or may affect other organ systems such as the respiratory tract or the skin, or the vascular system—alimentary allergy.

In the absence of reliable laboratory evidence and pathognomonic clinical signs the diagnosis of food allergy should only be entertained when organic or functional disorders of similar symptomatology have been excluded. On the other hand, unless the possibility of a hypersensitivity reaction to food has been considered, such a diagnosis cannot be made.

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TOPICAL THERAPY IN OTITIS EXTERNA

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In acute external otitis infection is rarely the one and only factor concerned. Often infection has occurred because of an existing disturbance of the meatal skin or environment. Adequate therapy must therefore take into consideration the host factors as well as the pathogens.

HOST FACTORS AND THERAPY

Normal skin has a slightly acid pH, often referred to as the 'acid mantle'. When the acid pH is replaced by an alkaline pH, resistance to bacterial and fungal invasion is impaired. Normal ear canals have a skin pH value chiefly within the acid range, whereas in external otitis the pH ranges between 7.1 and 7.8, well on the alkaline side. Indeed, it is not uncommon to find that of two apparently similar agents the effective one produces a state of acidity, whilst the ineffective one produces alkalinity.

During the summer the incidence of external otitis shows a sharp increase. This particularly involves swimmers, and the term 'swimmer's ear' has often been applied. Retention of moisture is probably to be blamed and removal of moisture from the infected skin is therefore important. Such a drying action in topical medication can be supplied by incorporation of alcohols, as for instance ethyl alcohol, glycerol, propylene glycol, and thymol. The high temperature may also contribute to swimmer's ear. It has been suggested that the combination of heat and moisture causes changes in the chemistry of cerumen and leads to dysfunction and plugging of the ceruminous glands. This in turn leads to scratching and rubbing and so predisposes to infection. It is essential that debris be thoroughly removed before applying ear-drops. Topical preparations which contain a wax-softening agent, such as propylene glycol, or those which contain a surface-wetting agent should therefore have an advantage over others. Many practitioners favour the use of a wick to promote contact.

Otitis preparations often contain topical steroids for anti-inflammatory effect. The use of steroids in this fashion, however, has a definite drawback: they mask manifestations of disease. In practice, therefore, only if one is sure about the antimicrobial agent can the less essential anti-inflammatory steroid be included. Some preparations contain local anæsthetics, but the use of local anæsthetics should probably be condemned because of their allergenic properties. Preferably, one should use a general analgesic such

as codeine during the first twenty-four hours of therapy. Beyond that, inflammation and pain will have greatly subsided if the antimicrobial therapy was effective.

Bearing in mind all these factors will often spell the difference between the success or failure of topical therapy. In summary, they are:—

(1) Acid pH.
(2) Absence of moisture.
(3) Reach the site of infection by removing debris, excessive wax and the use of a preparation with low surface tension.
(4) Avoid sensitizing agents, especially local anæsthetics.
(5) Do not mask the infection by the use of steroids when the correct choice of antimicrobial agent is in doubt.

PATHOGENS AND THERAPY

It is, of course, imperative to do away with the infection itself. If one is not obviously dealing with such non-infectious conditions as seborrhœic dermatitis, psoriasis or eczematoid dermatitis, it is fair to assume that infection is present and that it must be eradicated. The most common causative organism is *Pseudomonas pyocyanea*, which is involved in about 60 per cent. of all cases. True fungus infections of the ear are relatively rare. Among them, *Aspergillus niger* appears to play a dominant role, but other bacteria and fungi may be incriminated, and amongst each species one finds antibiotic-resistant strains. Bacteriological diagnosis and bacterial sensitivity testing is therefore theoretically desirable for the choice of the proper antimicrobial agent. Such a procedure, however, is usually impractical, inconvenient and costly and involves the loss of valuable time. This situation forces the practitioner to gamble and to pick at random from a number of available preparations, hoping that his choice will provide the right antimicrobial agent. Unfortunately, antibiotics, sulphonamides and nitrofurans, while potent, have limited antimicrobial spectra; and they may sensitize the meatal skin. New antibiotics which prove effective today may no longer be effective tomorrow because of the emergence of resistant strains.

A NON-ANTIBIOTIC FORMULA

Many older physicians with experience of antibacterial therapy in the pre-antibiotic days continue to rely on a non-antibiotic formula which is often useful even in otherwise resistant cases. They employ 2 to 5 per cent. solutions of an organic acid in alcohol: a favourite prescription is 5 per cent. acetic acid in ethyl alcohol. Such a mixture is used both for prevention and for treatment of external otitis. Unfortunately, the solution quickly evaporates from the ear and thereby loses its effectiveness. The combined action of acid with alcohol, however, apparently results in a wide antimicrobial range. As effectiveness without the use of antibiotics is a desirable feature, we have tested the merits of this principle using a less volatile alcohol.

In the solution we employed, acetic acid was retained as the organic acid. Acetic acid is well tolerated and many bacteria and fungi are unable to

metabolize it. Further, at equal pH it shows greater antibacterial properties than mineral acids such as sulphuric acid. Propylene glycol (propanediol) was chosen instead of ethyl alcohol because of its slower evaporation and because of its cerumen-softening action. To make a stable solution, acetic acid and propylene glycol cannot be simply combined as the two agents go into chemical reaction and a number of esters are formed. This problem is overcome by starting out with the di-ester and adding balanced amounts

Bacterial action						
Micro-organism		Culture control	Contact time 15 seconds	30 seconds	1 minute	5 minutes
Staphylococcus aureus 209		+	—	—	—	—
Staphylococcus aureus hæmolyticus 80/81		+	—	—	—	—
Staphylococcus albus 9491		+	—	—	—	—
Streptococcus mitis 6249		+	—	—	—	—
Streptococcus pyogenes M-34		+	—	—	—	—
Pseudomonas pyocyanea 'B'		+	—	—	—	—
Proteus vulgaris 190		+	—	—	—	—
Salmonella anatum M-49		+	—	—	—	—
Salmonella typhi P38A	R	+	—	—	—	—
K. pneumoniæ 'Ka'	R	+	—	—	—	—
Diplococcus pneumoniæ I 6301	R	+	—	—	—	—
Candida albicans 10231		+	—	—	—	—
Proteus vulgaris (Reilly)		+	—	—	—	—
Pseudomonas pyocyanea (Jones)		+	—	—	—	—
Aerobacter aerogenes (Pinkerton)		+	—	—	—	—
Micrococcus pyogenes aureus Y-1		+	—	—	—	—

Minimum fungistatic concentrations	
	Inhibitory concentration of propanediol acetic acid (percentage)
Candida albicans (Monilia)	4.15
Nocardia asteroides	2.07
Cryptococcus neoformans	4.15
Phiolofora pedrosi	2.07
Trichophyton rubrum	1.03
Trichophyton sulfureum	1.03
Trichophyton mentagrophytes	1.03
Sporotrichum schenki	4.15

To determine bactericidal action 0.5 ml. of 24-hour culture was added to 5 ml. of propanediol acetic acid. + = growth in subculture. — = No growth in subculture. R = Antibiotic-resistant strains.

TABLE I.—Antimicrobial spectrum of 'vosol otic solution'.

of acetic acid and propylene glycol. We have employed a stable system of this type containing 2 per cent. acetic acid, 3 per cent. of ester in the form of 1,2-propanediol acetate, and 95 per cent. of propylene glycol. When in contact with moisture, the ester slowly picks up water and releases acetic acid and propanediol, thereby keeping the acidity fairly constant. The antimicrobial range of this 'propanediol-acetic acid system' is virtually complete; *in vitro*, it proved to be bactericidal against all pathogens tested and commonly found in the ear (table I).

CLINICAL RESULTS

Such a preparation is now available under the name of 'vosol otic solution'. Its formulation is as follows:—

1,2-propanediol diacetate	3.0 per cent.
Acetic acid	2.0 per cent.
Benzethonium chloride	0.02 per cent.
Propylene glycol	to 100.0 per cent.

It was given an extensive trial in the United States last summer, and reports have been received from otolaryngologists of its use in 5,311 cases of otitis externa. A review of these shows that 'excellent to good' results were obtained in 94.6 per cent., and 'fair' results in 4.5 per cent., the preparation proving ineffective in only 0.9 per cent. In reports from individual otolaryngologists the incidence of 'excellent to fair' results ranged from 75 to 100 per cent. The only suggestion of sensitization was that two cases were reported of dermatitis in and around the meatal orifice, which disappeared when the preparation was withdrawn.

A field trial such as this has obvious limitations when it comes to interpreting results. Physicians will differ in their appreciation of contributing factors and in details of treatment. We accepted that all patients had external otitis; most of these were acute, some chronic; possibly a few were not of infectious origin. Reports of 'cures' and of 'excellent' or 'good' results were taken to mean about the same thing and were tabulated under one heading. Results reported 'fair' have been shown as such; at times this meant that prolonged therapy was required or that otitis recurred when treatment was stopped.

It came as somewhat of a surprise that a simple preparation such as this could be so effective. The never-ceasing flow of new antibiotics, their various combinations and their combination with steroids tend to make one overlook simpler methods. The one reported here offers a wider antimicrobial range and is fraught with fewer pitfalls than antibiotic therapy. It is unlikely that resistant strains will develop and sensitization must be a rare occurrence. The solution is acid and maintains acidity; it has the hygroscopic properties of propylene glycol, and the latter also permits better penetration because of its cerumen-softening action.

Prevention.—Finally, a word about prevention of otitis, especially among swimmers and campers. Obviously, antibiotics, and especially steroid-containing preparations, are not suitable for prophylactic therapy as their use would invite sensitization and the emergence of resistant strains. In contrast, a well-tolerated antimicrobial system of the type presented here could well be used day after day and retain its effectiveness while giving adequate protection.

SUMMARY

Details are given of a new preparation ('vosol otic solution'), containing acetic acid, for the treatment of otitis externa.

A survey, based on reports of 5,311 cases treated in the United States last summer, shows that it proved effective in 94 per cent. of cases.

A TRIAL OF A NEW COMPOSITE SULPHONAMIDE IN YOUNG CHILDREN

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DURING recent years the sulphonamides, although effective in the treatment of many infections, have lost their pride of place to the antibiotics. Many attempts have been made to produce preparations with a prolonged action allowing of smaller and less frequent dosages. 'Dosulfin', a composite sulphonamide containing equal parts of sulphaproxyline and sulphamerazine, has such a property.

SCOPE OF INVESTIGATION

During the latter half of 1958 we decided to substitute 'dosulfin' for the standard sulphonamide preparation already in use in the ward. We made

Diagnosis	'Dosulfin' group	Control group
Acute upper respiratory-tract infections	10	4
Bronchitis	17	12
Bronchitis with asthma	4	
Broncho-pneumonia	14	7
Lobar pneumonia	10	1
Urinary infection	5	—
Cervical adenitis; tonsillitis; sinusitis; otitis media	5	3
Tracheitis; cerebral thrombophlebitis	2	1
	67	28

TABLE I.—Diagnoses in group of patients treated with 'dosulfin' and in control group.

no attempt to lay down rigid rules for the use of the drug but suggested that the sulphonamide alone might be used in cases of tonsillitis, otitis media, urinary infection and mild upper respiratory infection and bronchitis should the resident in charge of admissions decide that a sulphonamide or antibiotic was required. A single, or once repeated, large dose of penicillin followed by 'dosulfin' was recommended for cases of broncho-pneumonia, lobar pneumonia and severe bronchitis but the registrar in charge (M.B.M.) could alter treatment at her discretion. The children admitted to another ward and supervised by one of us (M.B.M.) were used as the control group, penicillin being the drug of choice, with the addition of the standard sulphonamides as indicated.

A total of 67 children was included in the investigation: 42 boys and 25 girls. Of these, six were under 3 months of age, 20 were aged 4 to 12 months, and 11 were between the ages of 1 and 2 years. Diagnostic details are shown in table I. The 21 cases of bronchitis included four moderately severe cases of tracheobronchitis occurring in the first six months of life.

We attempted to isolate the organism in 58 of the 67 cases with the results shown in table II. There were several swabs from which no growth was obtained, but many of the children had received treatment with sulphonamides or antibiotics before admission to hospital. In addition, we were not able to undertake any virus studies.

Organism	'Dosulfin' group	Control group
Normal swab	17	10
Streptococcus viridans	9	3
Staph. pyogenes	7	3
Hæmolytic streptococci	8	4
E. coli	4	—
Pneumococcus, yeast hæmophilus	4	3
No growth	9	1
	58	24

TABLE II.—Organisms isolated in patients in whom bacteriological investigation was carried out.

TREATMENT

The dosage of 'dosulfin' was 0.2 g. eight-hourly during the acute phase followed by 0.1 g. eight-hourly, during the first year of life, with corresponding increase of dosage during the subsequent years. This was based on an average initial dose of 0.1 g./kg. body weight per day, with a somewhat higher dose in the first year and a lower dose in the older children.

'Dosulfin' alone was given to 19 patients. It was mainly used for cases of upper respiratory-tract infection, bronchitis and urinary infection. 'Dosulfin', plus an initial dose of penicillin (either a single or once repeated large dose [0.5 to 1 mega unit] intramuscularly), was given to 33 patients, consisting of the more severe cases of bronchitis and pneumonia, particularly in the younger age-groups. Combined therapy with 'dosulfin' and penicillin was given to the eight patients with severe bronchitis, pneumonia, laryngotracheitis and sinusitis. The broad-spectrum antibiotics were added (or substituted) in four cases of pneumonia (aged $2\frac{1}{2}$ to 5 years): one child had a severe kyphoscoliosis, in two children the lesion was slow to resolve and the parents of the fourth child had lost two children due to pneumonia, and oxytetracycline was started after the 5-day course of 'dosulfin' as a precautionary measure. In retrospect we feel that these children probably would have recovered without the added antibiotic. A fifth child had a

severe pneumonia for which chloramphenicol was prescribed and this drug also was given to a 4½-month-old baby with tracheobronchitis. The last child had a urinary infection which relapsed and oxytetracycline was added to the 'dosulfin' therapy.

The controls were all cases of respiratory-tract infection; the age distribution was somewhat different as there was a greater proportion under two years of age. The routine treatment was twice-daily penicillin by the intramuscular route until the temperature settled, followed by oral penicillin V for a few days. 'Sulphatriad' was also used in two cases and oxytetracycline in three cases.

Discharged from hospital	'Dosulfin' group	Control group
Within 7 days	41 (72%)	11 (40%)
Within 14 days	56 (83%)	24 (85%)
Within 20 days	60 (88%)	28 (100%)
Within 30 days	67 (100%)	—

TABLE III.—Length of stay in hospital in both groups of patients.

RESULTS

The progress of the children in hospital was satisfactory; they all recovered from their infections and developed no complications. We were able to return them quickly to their homes (table III), 83 per cent. of those in the 'dosulfin' series having left hospital within fourteen days of admission.

The drug was palatable and well tolerated and the only complication of 'dosulfin' therapy was some impairment of the ability to concentrate and dilute urine in three of seven cases tested in this manner. This was noticed when the drug was being administered but it disappeared two to three days after the cessation of treatment.

CONCLUSION

From these observations it would appear that 'dosulfin' (a composite sulphonamide containing equal parts of sulphaproxyline and sulphamerazine), given on its own or with penicillin, is an effective and safe drug in the treatment of respiratory-tract infections in young infants and of certain other infections in older children.

THE CARE OF CHILDREN'S TEETH

By J. H. GARDINER, B.D.S., D.Orth.R.C.S.

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At two years of age, approximately 40 per cent. of children have carious teeth (Slack, 1955), so that the practitioner may well be the first person to advise the parents upon the dental needs of their child. In addition to any discomfort brought about by dental caries, the actual appearance of prominent or irregular teeth can affect the happiness and outlook of children, as is well illustrated in the two following cases.

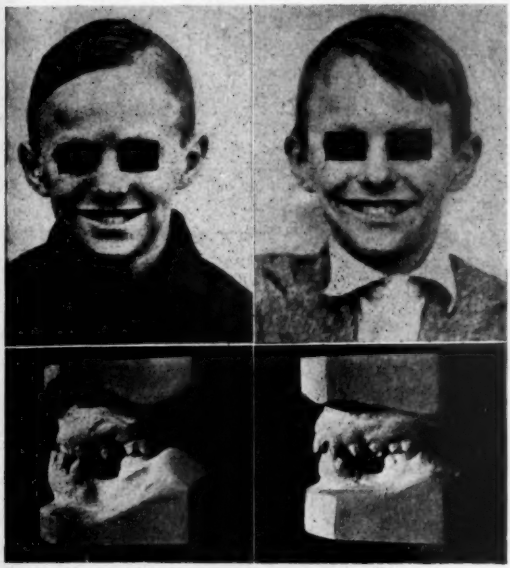
Case P.L. (White, Gardiner and Leighton, 1954) was a rather unhappy, undersized boy of nine years with a slightly prominent lower jaw (fig. 1a). This brought him ridicule from his playmates and, as he had difficulty in chewing, admonition from his father and schoolteacher, who both thought that the boy's dental condition was due to a mannerism. As a result of fifteen months' orthodontic treatment, his upper front teeth were moved forward so that his lower teeth could bite against them more effectively and he was able to hold his lower jaw in a more normal position (fig. 1b). Following the completion of treatment, his father paid a special visit to tell how the boy in recent months had 'brightened up' at home, how his school reports had improved, how he could now chew meat and, in contrast to his once retiring nature, how he could now 'lick any kid in the street'.

Case M.H. was an older boy with prominent upper teeth (fig. 2a), which had earned him the nickname of 'Bunny' at school; he also was retiring and fearful. One year's orthodontic treatment altered not only his appearance (fig. 2b), but also his nature and outlook.

THE MOUTH OF THE INFANT

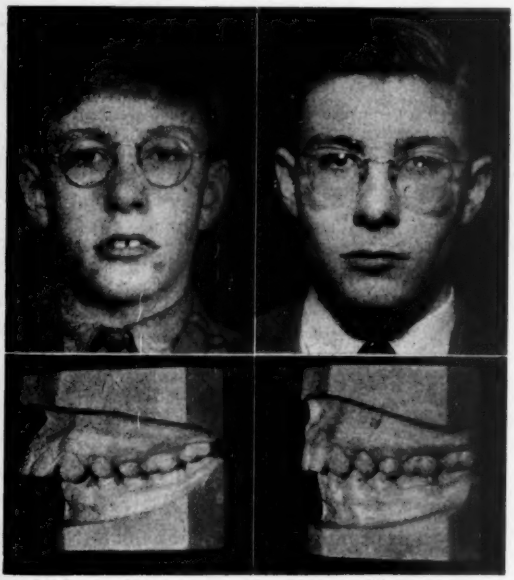
At birth the child's gum pads are not unlike the edentulous jaws of an old person. Very occasionally, one or more of the deciduous teeth may erupt prematurely and be visible at birth. This occurs in approximately one in every 2,500 live births. In my own 12 cases, and in 21 of the 24 cases reported elsewhere (Massler and Savara, 1950), these have been teeth of the normal deciduous series. Inheritance is an important etiological factor: over 40 per cent. of the cases reported had parents or siblings with the same anomaly. These teeth, being about six months premature in their eruption, have no root formation and therefore bend backwards when the child bites upon any object. For this reason they do not traumatize the maternal breast tissue as much as one would imagine. As these are teeth of the normal series, they are best left to develop, but if they produce persistent ulceration on the under-surface of the tongue, extraction would be justifiable.

In the infant the frenum labium appears large in comparison with that of an adult and may occupy a groove in the upper gum pad. It is, however, within normal limits and as the child's alveolar process grows downwards, so the frenum appears more normal. Should the frenum remain large and any operative interference prove necessary, this is better performed at the age of twelve years.



(a) (b)

FIG. 1.—Patient with prominent lower teeth: (a) before treatment and (b) after 15 months' orthodontic treatment.



(a) (b)

FIG. 2.—Patient with prominent upper teeth: (a) before treatment and (b) after 12 month's orthodontic treatment.

THE DECIDUOUS DENTITION

In figure 3 are seen the jaws of a child of seven years in which the buccal alveolar plate has been dissected away to show the close relationship between the developing permanent dentition whose crowns only are present (for the roots will not be fully developed until approximately twelve years of age), and their deciduous predecessors whose roots are just beginning to show resorption. If, due to caries, these latter teeth are lost before the permanent successors erupt into their places, then some collapse of the lower arch may take place and the permanent teeth become impacted. Owing to the intimate contact of the developing premolars with the roots of the deciduous molars, another complication following early caries in the deciduous molars is the accidental removal of the partially formed crown of the developing premolar, should the deciduous molars require extraction before the age of about six years.

DENTAL CARIES

The most widely accepted theory of the causation of dental caries is a modified form of Miller's chemico-parasitic theory, namely that bacteria acting upon fermentable carbohydrates on the tooth surface produce organic acids capable of dissolving the inorganic portions of the tooth.

The usual sites for caries to begin are the biting surfaces and those surfaces in contact with neighbouring teeth as, in these situations, food tends to collect and decompose. Bacterial action (especially of *L. acidophilus*) within these food plaques breaks down sugars and other carbohydrates into an acid which decalcifies the hard enamel surface of the crown. Once the enamel cap has been penetrated, the process spreads rapidly in the softer dentine and so undermines the enamel. Up to this stage, the carious process is almost invisible to the naked eye and can only be detected radiographically or with a sharp dental probe. The child, however, may begin to experience discomfort, especially following the consumption of sugar, owing to the increased osmotic pressure produced upon the dentine. In time the carious process irritates the pulp of the tooth, causing increased toothache until the pulp eventually dies. Subsequent infection of the dead pulp produces the well-known dental abscess.

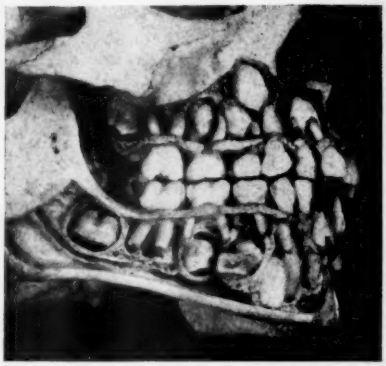


FIG. 3.—Dissected jaws of a child of seven years (from a preparation in the School of Dental Surgery, University of Sheffield).

Effect of reducing the intake of sweets.—Undoubtedly resistance to dental caries can be inherited, but it is known that children in institutions, as a rule, have a much lower caries frequency than children of the same social class living in their private homes in the same vicinity (Toverud, 1951).

One group of 51 orphanage children showing a very low caries rate were given up to half a pound (250 g.) of sweets daily for five months without changing the other foods (Jay, Hadley and Bunting, 1936), and this resulted in an increased *L. acidophilus* count with increased caries in most of the children. When the sweets were withdrawn, caries activity and *L. acidophilus* counts decreased.

In an older group of 500 with an average age of 31 years, in the Vipeholm Mental Hospital in Sweden, when each was given in their ordinary food three times the average sugar consumption per person in Sweden, it was found that the caries rate remained unaltered. When, however, half that amount of sugar was given in the food and the other half between meals in the form of sticky sweets, caries frequency increased considerably (Vipeholmsundersökningarna, 1950).

From Norway, Alexander (1950) has contributed some interesting figures (table I) showing the changes in the caries incidence in the permanent teeth of seven-year-old village children, when sweets were not available from 1942 until the end of the war. One simple preventive measure is

therefore to limit the consumption of sweets to a certain period each day when the child will have an opportunity of cleaning his teeth subsequently.

Effect of diet and nutrition.—Alexander (1950) points out that the results shown in table I may also have been influenced by improved diet, for those children up to six years of age, together with pregnant and nursing women, had received a fairly liberal amount of 'protective foods'. In England, Mellanby in 1934 emphasized the importance during the calcifying period

Year of examination	Number of carious surfaces per child	Years of assumed pre-eruption mineralization
1939-40	3.9	1931-32 to 1937-38
1940-41	3.0	1932-33 to 1938-39
1941-42	2.3	1933-34 to 1939-40
1942-43	1.4	1934-35 to 1940-41
1943-44	0.9	1935-36 to 1941-42
1944-45	0.8	1936-37 to 1942-43
1945-46	0.6	1937-38 to 1943-44
1946-47	0.6	1938-39 to 1944-45
1947-48	1.2	1939-40 to 1945-46

TABLE I.—The effect of wartime shortage of sweets upon the dental caries incidence in seven-year-old village children in Norway.

of vitamin D, calcium, and phosphorus in reducing dental caries, and Mellanby and Mellanby (1948) reported that the percentage of caries-free five-year-old London schoolchildren was 4.7 in 1929, 24.2 in 1943, 28.1 in 1945, and 37.5 in 1947. They suggest that this improvement is due to 'the increased calcifying properties of the dietary of this country and particularly that of pregnant and nursing women and infants and young children'. In addition to diet, care of the general health has been shown by Toverud (1948) in the Skedsno and Oslo health clinics to reduce the incidence of dental caries.

FLUORIDATION

According to one eminent dental authority (Wilkinson, 1955) fluoridation is 'undoubtedly the most significant advance that has been made in dentistry in the past few years'. Extensive investigations in the United States (Dean, 1954) and in this country (Weaver, 1944; Ministry of Health, 1955) have shown that children born and brought up in an area with about one part per million of fluoride in the domestic water supply have 50 to 60 per cent. less dental caries than those brought up in areas where the water is deficient in fluoride. The artificial addition of fluoride (usually in the form of sodium fluoride) to produce one part per million of fluoride in the public water supplies previously totally deficient in fluoride, has been shown to produce the same dramatic results over a 6½-year investigation (Arnold *et al.*, 1953).

In those areas where the water supply is deficient in fluoride the obvious remedy is to increase it, and it is regretted that in this country the necessary measures to do this may take some years to come about. An alternative method of administration is to give tablets containing sodium fluoride

(Held and Piquet, 1954) to infants, children, and expectant and nursing mothers, and yet another method is the application of a 2 per cent. sodium fluoride solution to the surface of the teeth. In large-scale studies Knutson (1948) and others have shown that a caries reduction of between 25 per cent. and 50 per cent. was possible in children and young adults by this latter method. As young enamel is more permeable than old, Knutson recommends four applications of sodium fluoride at intervals of a week at 3, 7, 10 and 13 years.

ORAL HYGIENE

Besides such general measures as diet and fluoridation, the prevention of dental caries can be influenced by simple cleanliness (Fones, 1927).

In Bridgeport, U.S.A., for ten years Fones concentrated on maintaining a high standard of oral hygiene in 10,000 schoolchildren; the other 10,000 children under his charge were examined only periodically and acted as a control. A specially trained team of 26 nurses not only cleaned the test-group children's teeth when necessary, but also instructed them in toothbrushing routine, diet, and the like, and by regularly visiting the schools of these 10,000 children under investigation, they ensured that a high standard of oral cleanliness was maintained. After ten years Fones discovered that the amount of dental caries in the test group fell from an average of 5.5 carious cavities per mouth to 2.5—a reduction of over 50 per cent.

Another investigator of the effectiveness of toothbrushing on reducing dental caries (Fosdick, 1950) used an older group of 523 students and, as a control, a further 423 students from various universities, the mean age of the former being 22.7 years and the latter group 23.7 years. The test students were given a brush and a dicalcium phosphate detergent dentifrice; they were instructed in an accepted technique of toothbrushing and asked to brush their teeth within ten minutes of eating foods, sweets, or sweetened drinks. The control students were told to continue cleaning their teeth as they did before. At the start, and after one year and two years of the investigation, the teeth of both groups were examined clinically and radiographically, and *L. acidophilus* counts were also taken. After two years the test group had 41 per cent. fewer new cavities by clinical examination and 60 per cent. less by radiographic examination than the control group.

Toothbrushing should begin as soon as the first tooth appears in the baby's mouth at about six months, by using a soft badger-haired toothbrush and plain water or any dentifrice that the infant appears to enjoy. Later, at 3 to 4 years of age, the child should be able to brush his own teeth with a suitably sized soft or medium texture brush, provided he is given a low stool to enable him to reach the wash-basin, and also any training which inspection of his efforts shows to be necessary.

The old-fashioned horizontal piston-stroke toothbrushing action has been shown to have an adverse effect not only on the gum tissue, but also on the root of the tooth. A vertical action, brushing from the gum on to the teeth, not only cleans the teeth more efficiently, but also stimulates the gum tissue (Carter, 1956).

REGULAR VISITS TO THE FAMILY DENTIST

Another important measure is periodic dental inspection so that any break in the enamel surface by caries can be promptly checked at three-monthly intervals between the ages of 3 and 12, and half-yearly inspections thereafter, but the frequency will vary according to the individual child.

As approximately 40 per cent. of children have caries at 2 years of age (Slack, 1955), regular inspections should begin before the child's third birthday. Before the first visit it usually helps if the child is allowed to accompany a parent and to watch him receiving dental treatment; this is more inspiring to their young minds than a gruesome account by an elderly relative of some extractions they experienced in the 1918 Army without anæsthetic. Also, it is better that the child's first dental inspection should be before he has started school, as he is then less likely to have been primed by terrifying dental stories from his playmates.

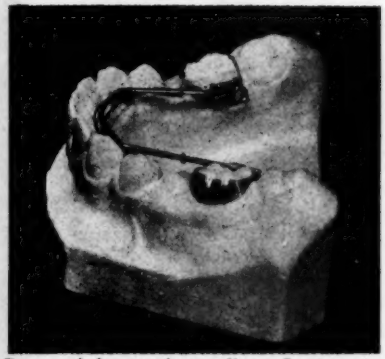


FIG. 4.—A lower wire appliance fixed to the teeth for moving the lower front teeth forwards.

TREATMENT OF CARIES IN THE VERY YOUNG

Should any dental caries be present in the child's mouth on the first visit, the most the dental practitioner is likely to do will be to paint the affected tooth surfaces with some solution such as ammoniacal silver nitrate (Prime, 1935). This has the effect of turning any affected dentine completely black and, when inspecting a child's mouth, should be differentiated from the browner colour of carious dentine. After the first visit it is better for the child to go into the dental surgery alone so that, having the full attention of the child, the dentist can more quickly win his confidence.

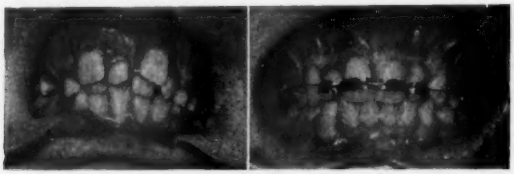
If a child's mouth has been so neglected that a deciduous molar has to be extracted and the resultant space begins to close, then it may be necessary to fit a small plate for wear at night to keep the space patent for the premolar.

ORTHODONTIC TREATMENT

In the event of a child's losing some deciduous molar teeth prematurely, the arch may to some extent collapse and it becomes necessary at about 10 to 11 years of age to fit either a screw plate which can be removed for cleaning, or a wire appliance fixed to the teeth (fig. 4) in order to restore the arch to its original size. Should such an appliance require to be worn, then tooth-cleaning measures must be redoubled, for although these appliances in themselves do not harm the teeth, they not only harbour fermentable food debris, but they also interfere with the natural cleansing action of the tongue, lips and cheeks.

Sometimes the deciduous teeth stay in position too long and cause the erupting permanent tooth to be diverted from its correct path of eruption. This usually results in the permanent upper incisors becoming locked behind the lower incisors and necessitates orthodontic treatment at about seven or

eight years of age for its correction. An appliance similar to that used today was first described by John Hunter in 1771. Aberrant eruption of a permanent tooth, especially the upper canine, can cause trauma to the neighbouring teeth and can also on occasion be responsible for vague neuralgia. Such an unerupted displaced tooth could either be extracted surgically or moved into its correct position by means of orthodontic treatment even at



(a) (b)

FIG. 5.—(a) Irregularity produced by extra teeth. (b) Same patient during treatment.

16 or 21 years of age. If an indication for orthodontic treatment is observed, it is better to refer the child to his own family dental practitioner who will, if necessary, refer him for specialist advice.

CARE OF THE PERMANENT TEETH

Permanent teeth begin to erupt at about 6 years and, apart from the third molars, have all erupted by 12 years of age. They are not only larger than the deciduous teeth, but have a thicker enamel covering and are darker in

(a) (b) (c)

FIG. 6.—(a) Eruption of upper permanent incisors delayed by seven years. (b) Teeth after uncovering surgically. (c) Final stages in the treatment.

colour. Regular brushing of these teeth is of even greater importance as these are the teeth which should last the child throughout the rest of his life. After 12 years of age dental inspections need only be at half-yearly intervals, but the dental practitioner may advise inspection more or less frequently, according to the child's susceptibility to caries.

Conservation of the permanent teeth.—To conserve the permanent teeth the dental practitioner usually employs more durable filling materials, such as silver amalgam, gold, plastic or silicate cement. The treatment of the carious portion of the tooth and its preparation to receive restorations is a skilled procedure, as the filling may have to withstand a biting force of over 100 pounds (45 kg.). Following the shaping of the cavity, a specially fine-

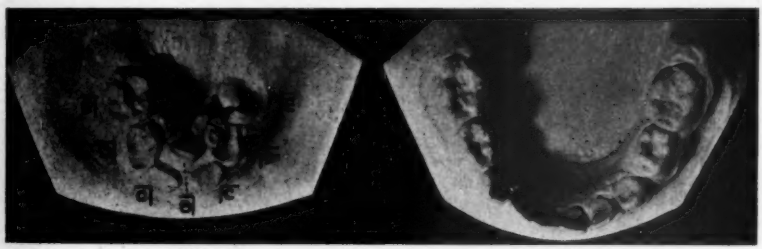
grained cement lining is placed upon its 'floor' to insulate the more sensitive portions of the tooth from heat conducted through the metal filling.

If the permanent teeth are not cared for, they will in most cases begin to ache and may be extracted indiscriminately. This may result in the neighbouring teeth drifting and can have a marked effect upon the opposing arch.

FIG. 7.—Congenital absence of several permanent teeth in a girl of twelve years.

Wilkinson (1953), in an unpublished survey of 112 dental students, found that 50 per cent. had lost one or more first permanent molars, and 77 per cent. of these showed malocclusion compared with 39 per cent. who had retained all the first permanent molars.

Fracture of the permanent teeth.—A blow or fall can result in the accidental fracture of an anterior tooth or its root, especially when these teeth are prominent, and it is important that such injuries should be seen immediately by a dental surgeon. If the fracture is slight and is confined to the enamel and radiographs do not reveal any fracture of the root, then the only treatment may be to smoothen the fractured surface. Should the dentine be exposed and be sensitive to hot and cold drinks, then this area can be



(a) (b)

FIG. 8.—(a) Lower teeth of a child with congenital aglossia. (b) Lower teeth of her more normal younger sister. (By kind permission of the *B.S.S.O.* and the *Dental Practitioner and Record.*)

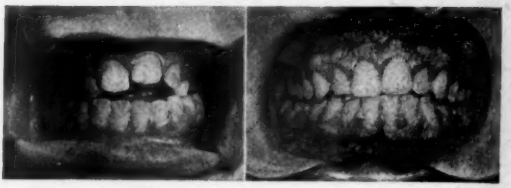
covered temporarily until the patient is 17 to 18 years of age, when a more permanent jacket can be made. Should the major portion of the crown of a front tooth be broken away, then the pulp of the tooth will become exposed and may have to be extirpated aseptically. In such a case the end of the root canal would be sealed with an antiseptic cement and a metal pin inserted, carrying a solid crown resembling the original in size, colour and shape. When the tooth is not fractured, but has been loosened by a blow, it is usually splinted to the adjoining teeth for some weeks.

SUPERNUMERARY TEETH AND ANODONTIA

Supernumerary teeth.—Teeth extra to the normal complement, or supernumerary teeth, occur in approximately 1 per cent. of the population, but

in only 0.3 per cent. are they erupted (Stafne, 1932). These can be responsible not only for irregularity of the erupting permanent teeth (fig. 5), but can delay the eruption of permanent teeth (fig. 6) and can cause a wide space to appear between the upper central incisors. Occasionally during development these extra teeth fuse with a tooth of the normal series, producing one very large tooth.

As mentioned previously, a median diastema between the upper permanent central incisors might occasionally be brought about by a large and fibrous frenum labium, but resection of the frenum is not recommended until the child reaches 12 years of age, for by then these teeth have usually moved together as a result of natural dental development.



(a) (b)

FIG. 9.—(a) The effect of thumb sucking upon the anterior teeth. (b) Same child after treatment.

Congenital absence of teeth.—Congenital absence of teeth or partial anodontia occurs in about 3 per cent. of the population (Dolder, 1936) and usually consists in the absence of a single permanent tooth which may scarcely be noticed. More extensive cases of anodontia are rare, but can affect the patient's appearance and outlook adversely (fig. 7). Congenital aglossia is exceedingly rare, but when it occurs, it can have a profound effect upon the lower dental arch (fig. 8), thus illustrating the influence of the cheeks, lips and tongue upon the arrangement of the lower teeth (Gardiner, 1960).

(a) (b)

FIG. 10.—(a) An unoperated unilateral cleft in a patient of fourteen years. (b) Collapse of the upper arch following surgery unassisted by orthodontic treatment.

HABITS WHICH PRODUCE DENTAL IRREGULARITIES

Thumb or finger sucking is almost inevitable at some period in children up to the age of 2, but thereafter diminishes with age and most children abandon the habit on starting school at 5 years of age. If the habit is continued after 6 years of age when the permanent incisors erupt, it may result in a prominence of the upper incisors and some retrusion of the lower incisors (fig. 9). It has been suggested (Ballard, 1959) that this is more likely to occur when there is a hereditary predisposition to prominent upper teeth.

In a survey of 1000 unselected schoolchildren (Gardiner, 1956) it was found that only 14 per cent. of those children who suck thumbs or fingers do in fact produce an irregularity of their teeth.

Should this latter occur, initiation of orthodontic treatment, especially when a dental plate covers the palate, is usually accompanied by cessation of the habit. It has been noticed (Gardiner, 1956; Townend, 1956) that children who received a comforter in infancy are less likely to develop a thumb- or finger-sucking habit later, and a comforter has the advantage that it can be thrown away after 3 to 4 years. It should not, however, be smeared with

(a) (b) (c)

FIG. 11.—(a) Frontal view of an infant at birth suffering from a total unilateral cleft of primary and secondary palates on the left side. Note the deflection of the nose towards the non-affected side. (b) Same infant following orthodontic treatment only. (c) Same infant following surgical lip repair. Note especially the balance of the nose. The red margin of the lip can be attended to at a subsequent operation. (By kind permission of Dr. W. R. Burston and the *Dental Practitioner and Record*.)

honey, or the like, for then gross caries would occur in the upper incisor teeth.

An open-mouth condition is not necessarily associated with mouth-breathing.

Indeed, in one investigation (Warwick James and Somerville Hastings, 1932), it was discovered that only 6 per cent. of children with an habitually open mouth did in fact breathe only through the mouth, a further 13 per cent. breathed through both nose and mouth, and the remaining 81 per cent., even though they consistently held their mouths open, actually breathed entirely through the nose.

Very often a perpetual open mouth is in no way associated with a nose or throat condition and may be a temporary phase, extending sometimes into early adolescence, or it may be permanent (Ballard, 1952). In other children, an earlier thumb-sucking habit may cause such a prominence of the upper incisors that the child is unable to approximate his lips.

SPEECH DEFECTS AND THE TEETH

Although some children with a speech defect may have irregular teeth, the converse is not necessarily true and, in fact, authoritative investigation would indicate that it is rarely so.

Van Thal (1935) examined 180 orthodontic patients, 90 per cent. of whom had speech defects in a varying degree but, although she felt that a poor dentition has an

unfavourable effect on speech, it was not the actual cause of such defects as lisping. Bernstein (1954) investigated 437 children with defective speech and compared them with a control group of 446 children with normal speech. A statistical analysis of his results showed speech defects not to be related to malocclusion apart from the condition of open incisor bite, which he felt had a relationship with lisping, but the degree of lisp was not related to the extent of the open bite.

CLEFT PALATE TREATMENT AND THE TEETH

Whilst pædiatric and plastic surgery can do so much to reconstruct a cleft palate, it is often followed by gross deformities of the deciduous and permanent dentitions (fig. 10), which can prove most intractable to orthodontic treatment. Investigations by McNeil (1954) and by Burston (1958) have shown that the collapse of the anterior portion of the maxilla, so often seen in cleft palate patients, can be corrected preoperatively. This treatment results in a firm foundation around which the surgeon can reconstruct the lip and nares (fig. 11).

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GENERAL PRACTITIONERS' FORUM

THE ARTIFICIAL FEEDING OF INFANTS

By P. D. MULKERN, M.R.C.S., L.R.C.P.
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'Nothing is easier than to overfeed and overfatten a baby by such means [patent baby foods] . . . Such children are seriously handicapped for life and lack the well-balanced normal proportionate development of muscles, bones, teeth and internal organs which only breast feeding can establish to perfection during the first six months or more after birth'.—Sir Truby King.

For many reasons mothers are no longer giving their babies the breast milk that was intended for them. Perhaps ten per cent. are fed in this way. Of the remainder, about half fail to lactate for longer than one month and the other half suppress the milk with the connivance of the nurse and doctor because artificial feeding is so convenient and they are too busy to breast feed. The commercial production of conveniently hygienic dried milk powder has conditioned the doctor to accept with confidence the necessity for dispensing with lactation should any doubt or difficulty arise. When it is

	Units per 100 ml.	Human	Cow
Water	grammes	88	88
Protein	,,	1.5	3.5 to 4
Carbohydrate	,,	6.5	4.75
Fat	,,	4	3.75
Calories		63 to 74	66
Calcium	mg.	34	122
Phosphorus	,,	15	90
Iron	,,	0.07	0.03
Copper	,,	0.06	0.03
Magnesium	,,	13	6
Chloride	,,	116	58
Sulphur	,,	31	15
Sodium	,,	61	31
Potassium	,,	154	77

Table I.—The composition of milk (Dean, 1953).

realized, however, that full-cream dried milk powder, whether of proprietary brand or the National type, is dehydrated cow's milk, and further that recomposition in accordance with the tables stamped on the tin creates a liquid equivalent to cow's milk, it is time to start thinking and to retrace our steps back to the early days of artificial feeding when 'humanized' milk was advocated.

THE COMPOSITION OF MILK

The composition of cow's milk and 'human' milk is shown in table I, and the

relative proportions of the three main constituents—protein, carbohydrate and fat—are shown in figure 1.

Protein.—This is composed of caseinogen and lactalbumin in different proportions (table II, fig. 2).

Caseinogen is both relatively and absolutely less in human milk than in cow's milk because the cow grows four times as fast as the baby and requires

FIG. 1.—Composition of human and cow's milk.

more protein for body building, as well as more calcium and other salts. Caseinogen contains practically all the amino-acids necessary for building up body proteins except glycine, which can be synthesized, and cystine, which is present in lactalbumin. If protein is given in excess of requirements or, in other words, if we advise mothers to feed their babies as if they were calves, we must allow for the following possibilities. Whole dried cow's milk

Milk	Percentage of Protein	Percentage of Caseinogen	Percentage of Lactalbumin
Cow's	4	2.8	1.2
Human	1.5	0.55	0.95

TABLE II.—The protein content of cow's milk and human milk.

feeding supplies 28 per cent. of protein instead of the 12 per cent. found in human milk.

Protein stimulates metabolism 20 per cent. in contrast to the 5 per cent. or 6 per cent. stimulus by fat and carbohydrate. In fact it has a drug-like action which increases hunger and growth four times more effectively than fats and carbohydrates. This means that babies fed on whole cow's milk, whether fresh or dried, will develop an appetite for more and will grow faster. Growing body bulk itself increases metabolism and creates hunger.

FIG. 2.—Protein components of human and cow's milk.

More milk is required to meet it and this again carries the demand higher owing to the disproportionate protein content. A vicious circle ensues. In a healthy vigorous baby this strain on the digestive capacity and on the metabolic processes associated with active development can be met without fault, but will cause a breakdown in the resources of a weaker infant beset

by inherited or environmental defects. Selye (1950) has pointed out that 30 per cent. of protein is the maximum normal acceptable amount and that stress factors affect animals in direct proportion to the percentage of protein in the diet, causing the general adaptation syndrome and hypertrophy of the adrenal cortex. Do we not see moon-faced babies produced by dried milk feeding to excess? In simple terms this means that high protein feeding will cause babies to react by fever, catarrh and inflammation to minor infections and will precipitate inherited defects such as eczema, asthma and acidosis. If, by deploying all available vitality, the baby remains healthy and thriving, as so many do, it still seems possible that steady development of the nervous system and of the emotional personality of the infant may be arrested, thus helping to create the behaviour disorders of insomnia, tantrums, anorexia nervosa, excessive motor activity, breath-holding and petit mal which are so puzzling in the later stages of babyhood.

Fat.—The fat of cow's milk consists of large globules of saturated fatty acids, the neutral glycerides, tripalmitin, tristearin and triolicin, as well as

	Cow's milk (per cent.)	Half-strength or dried milk (per cent.)	Human milk (per cent.)	Add to humanize (per cent.)
Protein	3.5	1.75	1.5	
Carbohydrate	4.75	2.4	6.5	4.0 (i.e. 60 grains in 3½ fluid ounces)
Fat	3.5	1.75	4.0	2.25 (i.e. 60 grains of 50% fat emulsion in 3½ fluid ounces)

TABLE III.—Conversion of cow's milk, half-strength or dried milk, and human milk to humanized milk.

the glycerides of butyric acid and of all other saturated fatty acids up to the carbon number of lignoceric acid. The volatile fatty acids, of which cow's milk contains seven times as much as human milk, are difficult for the baby to digest. Fat of human milk contains unsaturated fatty acids including 7 per cent. linolenic acid lecithin and cholesterol.

Carbohydrate.—The lactose of both cow's milk and human milk is the same and can be increased by simple addition for human babies.

Other properties of cow's milk.—Cow's milk is distinctly acid by the time it is prepared for artificial feeding and has a high buffering property making it difficult to digest. The large amount of casein curds and the small amount of albumin whey are in contrast to human milk. Moreover, whether fresh or dried, it is not free from bacteria as is breast milk.

HUMANIZED MILK

During the neonatal period breast milk contains a higher proportion of protein in the form of soluble lactalbumin and a lower percentage of fat.

By the end of the first month the mother's milk has become a standardized mixture and remains so until weaning takes place (Dean, 1953). In creating humanized mixtures there is no need to manipulate the percentages of the ingredients according to the age of the infant.

Table III demonstrates the changes required to make an approximate substitute for human breast milk from whole cow's milk, fresh or dried.

Full-cream dried milk can be reconstituted correctly as cow's milk by dissolving the powder in water to the proportion of 1 in 8. Proprietary or national brands of full-cream dried milk may therefore be used in half the strength advised on the tables supplied with each tin for a given amount of water diluent to create humanized mixtures. Humanized milk has a calorie value of 18 calories per fluid ounce. Babies require 40 to 50 calories per pound, which represents $2\frac{1}{2}$ fluid ounces of milk per pound per day. The baby's correct weight at any given date in weeks or months from birth can be calculated as:—

$$\text{Birth weight (in pounds)} + \frac{5 \text{ ounces (age [in weeks]} - 2)}{16}$$

Birth weight is usually doubled at six months and 20 pounds is a reasonable weight at one year.

The feeding procedures discussed in this article are intended for normal infants. The postmature, overweight infant born of a diabetic or pre-toxæmic mother should be given special consideration. Obesity or overweight

	Milk mixtures per four-hourly feed							
	Weight (pounds)	Cow's milk	Dried full cream (heaped teaspoonfuls)	Dried humanized (heaped teaspoonfuls)	'Kariol', 'Karilac' or 'Brestol' (teaspoonfuls per feed)	Water/Feed (ounces)		Total in 24 hours (ounces)
1st and 2nd weeks	7	$1\frac{1}{2}$	$1\frac{1}{2}$	3	1	2	$3\frac{1}{2}$	$17\frac{1}{2}$
3rd week	$7\frac{1}{2}$	$1\frac{3}{4}$	2	3	1	2	$3\frac{1}{2}$	$18\frac{1}{4}$
1st month	8	2	2	3	1	2	$3\frac{1}{2}$	20
2nd ,,	$9\frac{1}{2}$	$2\frac{1}{4}$	$2\frac{1}{2}$	$3\frac{1}{2}$	1	$2\frac{1}{4}$	4	23
3rd ,,	11	$2\frac{3}{4}$	3	$4\frac{1}{2}$	$1\frac{1}{2}$	$2\frac{3}{4}$	5	$27\frac{1}{2}$
4th ,,	$12\frac{1}{2}$	3	3	5	$1\frac{1}{2}$	3	6	30
5th ,,	14	$3\frac{1}{4}$	$3\frac{1}{2}$	$5\frac{1}{2}$	2	$3\frac{1}{2}$	$6\frac{1}{2}$	35
6th ,,	15	$3\frac{3}{4}$	4	$5\frac{1}{2}$	2	$3\frac{3}{4}$	$6\frac{1}{2}$	$37\frac{1}{2}$
7th ,,	$16\frac{1}{2}$	4	4	6	2	4	$7\frac{1}{2}$	40
8th ,,	18	$4\frac{1}{2}$	$4\frac{1}{2}$	7	$2\frac{1}{2}$	$4\frac{1}{2}$	$8\frac{1}{2}$	45

TABLE IV.—Method of calculating how much milk per feed is required. (The figure in the first half of the Water/Feed column is for fresh milk dilution and that in the second half for dried milk solvent. 'Kardiol' and 'karilac' are not used with dried humanized milk mixtures.)

in the neonate is not a sign of good health if born of a mother with a metabolic defect. Such infants should therefore be 'dieted' by feeding them according to a conceived ideal weight half-way between 7 pounds and their actual weight during the first two weeks, and thereafter according to their expected

or calculated weight. If fed according to birth weight their digestive and metabolic apparatus will be embarrassed and cause them to break down in some respect of health sooner or later. With this information to hand it is simple to calculate how much milk per feed any given baby requires; a sample table is given as a rough guide (table IV).

FRESH COW'S MILK FOR HUMANIZED MIXTURES

Some say there is an occult biological factor in fresh milk which is absent from dried milk powder. The former is certainly more palatable and less 'fatty', but it is more liable to contamination and cannot be stored without a refrigerator. It can have added a supplementary additive containing 50 per cent. of blended fats of composition almost identical with breast milk combined with 38 per cent. carbohydrate ('brestol'). Sixty grains are given separately with every 3½ fluid ounces of half-strength milk. Another preparation is New Zealand cream, which is 50 per cent. fat emulsion and 40 per cent. carbohydrate obtainable from Mothercraft Training Society Clinic, 193 Dyke Road, Hove 4, Sussex. Two-thirds of the fat is of animal origin from cod-liver oil and butter and one-third is of vegetable origin such as peanut oil. This is also best given as a separate supplement to the milk mixture. All that need be added to the prepared milk and water, equal parts, is about one teaspoonful of lactose or 'karilac' (dextrose and gelatin) in 3½ fluid ounces of milk mixture. To avoid hair-raising calorie calculations as to the ultimate value of all this, remember that the central milk and water mixture with its attendant supplements of cream and lactose still has a value of 18 calories per ounce.

DRIED MILK FULL-CREAM POWDER FOR HUMANIZED MILK

The drying process reduces the size of the fat globules. The cooking process also changes the taste and smell. Fat tends to appear as separate 'lakes' after the milk has been made up, but the vogue of full-cream dried milk is firmly established and can be used to make a humanized feed as recommended in the table. Lactose is added and supplementary cream is given before the feed.

HUMANIZED MILKS

There are on the market several brands of dried humanized milks which avoid the necessity for calculating supplementary fat and carbohydrate and eliminate the inconvenience of these additions to the feeding routine.

COST AND CONCLUSIONS

The most economical method of feeding is with dried milk supplied by the welfare division of the Ministry of Health. For the cost of another 2½d. a day, for a baby taking one pint, proprietary brands of full-cream dried milk can be used; if fresh milk is used the cost is slightly less. The prepared

brands of humanized milk are between two and three times as expensive to use, but are excellent in quality, easy to prepare and pleasant to drink.

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SULPHINPYRAZONE IN THE TREATMENT OF GOUT

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Treatment of the chronic gouty state, and of the intervals between acute attacks, makes use of uricosuric agents in an effort to prevent their recurrence. Lowering of the serum uric acid level by enhanced renal excretion has been variously reported, using aspirin, probenecid, and phenylbutazone. A proportion of patients, however, is intolerant of one or all of these agents and search was therefore made for more effective and less toxic uricosuric agents. Two such agents, which are derivatives of phenylbutazone, have been synthesized, and the more potent of the two, sulphinpyrazone ('anturan'), has now been made available for clinical use. Clinical reports have been favourable (Ogryzlo *et al.*, 1957; Kersley *et al.*, 1958; Roden, 1960; Hart and Burley, 1960), and so far no report has appeared of intolerance to it.

In this practice of 2,800 there are six known cases of gout of whom four were either unable to tolerate or did not derive benefit from the usual drugs. A trial was therefore made of sulphinpyrazone in these patients and their response is now reported.

CASE REPORTS

Mr. A., aged 55 years, is managing director of a large commercial undertaking who suffers from frequent disabling attacks of acute gout affecting the knees, ankles and feet. He is unable to attend to his numerous commitments during these attacks. This annoys him but pleases his subordinates. He is intolerant of colchicine, aspirin and probenecid. Each produces violent gastric pain and he has had to await spontaneous remission of each attack. Two years ago he was given sulphinpyrazone, 50 mg. thrice daily, during an acute attack, and much to his relief all inflammatory signs diminished rapidly during the next few days. He did not continue with the drug, however, until his next attack some weeks later when he again obtained relief without any hint of gastric upset. He consumes large quantities of spirits each day and masses of purine-rich foods, neither of which he is willing to forego. He has continued to take sulphinpyrazone at the onset of his acute attacks and when last seen, six months ago, he was delighted with the response.

Mrs. B., aged 67 years, has chronic tophaceous gout of the fingers of one hand. During an acute episode two years ago, because of her failure to respond to colchicine or salicylates, she was given sulphinpyrazone in 50-mg. doses four times daily. There was no immediate response, but after a week the joint swellings sub-

sided and thereafter she continued sporadically with a maintenance dose. When she stopped taking it temporarily some twelve months ago, her gout returned. She soon restarted taking the drug and has had no further attack since.

Mr. C., aged 66 years, suffers from gout involving the big toe. Attacks occurred every three months and he had gastric intolerance of colchicine or aspirin. Before a gastric ulcer was demonstrated he was given short courses of phenylbutazone,

(a)

(b)

FIG. 1.—X-rays of right hand of Mrs. D., taken (a) before the administration of sulphinpyrazone, and (b) two years later.

100 mg. thrice daily, which helped him. Two years ago he started on sulphinpyrazone in doses of 50 mg. thrice daily, which were later increased to 100 mg. thrice daily. He has had no sign of gastric intolerance to the drug and has had only one or two very minor attacks of gout since.

Mrs. D., aged 70 years, has been crippled with extensive chronic tophaceous

gout for many years. She lives alone and depends on a daughter who visits her daily. She was confined to her room and could spend only a few hours a day out of bed when she sat uncomfortably in a chair. The disease affected the spine, hip and knee joints, and the fingers and toes were gnarled grotesquely. Massive tophi overlaid her finger-joints and her fingers were in permanent flexion. She had taken aspirin for many years without apparent effect. During acute episodes she received colchicine and a trial was made of probenecid as interval treatment, again without noticeable effect. Two years ago she started on sulphinpyrazone, 50 mg. thrice daily, which was later increased to 100 mg. four times daily. Improvement since has been progressive, and she has had no further acute attacks. She can now stand erect, hobble with the aid of a stick, and has walked outside her flat during the last six months after many years of confinement to her room. Her hands and fingers have shown dramatic improvement (fig. 1). She now has full movement of all fingers and their joints, and the large tophi have shrunk and most have disappeared. Deformities of toes and feet have shown similar improvement. She is left at present with some minimal hip pain but is able to walk with the aid of a stick and perform her personal household duties.

SUMMARY

Clinical improvement with sulphinpyrazone ('anturan') is reported in four patients who suffer from gout. Previously they had not responded to, or were intolerant of, the usual uricosuric agents.

I wish to thank Dr. W. Stoddart of Geigy Pharmaceutical Co. Ltd., for the supply of sulphinpyrazone used in this trial, and for his help and advice; and Dr. M. Israelski for the radiographs.

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GENERAL PRACTITIONER CLINICAL TRIALS

TWO NEW ANOREXIANT DRUGS

'Filon'

ANOREXIANT properties have been claimed for a combination of two synthetic ephedrine derivatives, phenmetrazine theoclate and phenbutrazate hydrochloride ('filon', also known as 'cafilon' on the Continent).

SCOPE OF INVESTIGATION

This trial was undertaken by five members of the Group to measure the weight lost over three months, by patients taking this combination of drugs. The combination contains 30 mg. of phenmetrazine theoclate and 20 mg. of phenbutrazate hydrochloride per tablet, and the dosage used was

one to two tablets twice daily, taken first thing in the morning and at midday. A total of 64 patients was studied, the women outnumbering the men by 3 : 1, with the maximum incidence almost equally divided between the 31 to 50 years, and 51 years and over, age-groups. The majority of these patients were over 168 pounds (76 kg.) in weight, and 61 per cent. of them were in the 168 to 190 pounds (76 to 86 kg.) range.

RESULTS

At the time when this trial was undertaken, supplies of the compound were limited, and in consequence not all patients could be studied for the full

	Average 2-month weight loss						Number of patients on 'filon'	
	'Filon'		All others		Dexampheta-mine		Losing weight	Not losing
	Pounds	Kg.	Pounds	Kg.	Pounds	Kg.		
Dr. A.	5	2.3	6	2.7	6	2.7	5	3
Dr. B.	14	6.3	5	2.3	1	0.45	3	0
Dr. C.	14	6.3	10	4.5	11	5.0	7	0
Dr. D.	4	1.8	2	0.9	3	1.4	11	2
Dr. E.	7	3.2	16	7.3	6	2.7	10	1
Over-all average	9	4.1	8	3.6	7	3.2	36 (86%)	6 (14%)

TABLE I.—Comparison of reduction in weight following administration of 'filon' and other anorexiant drugs.

three months' period. In the first month of treatment, when the full 64 patients were treated, the average weight lost was 4 pounds (1.8 kg.), by the end of the second month this average loss had increased to 9 pounds (4 kg.), but by the end of the third month it had been reduced to only 5 pounds (2.25 kg.). This was the average weight lost for the full three months, in those patients who completed the full course of treatment. These third-month figures are probably not of much significance, since the cases completing three months were comparatively few in number. They suggest, however, and this was also apparent from studying individual patients, that weight loss tends to slow up in the third month. This is quite a usual experience with anorexiant drugs, and the second-month figures are probably the most useful for obtaining a comparison with previous forms of treatment. Of the patients in this trial, 46 (68 per cent.) had previously been treated with other anorexiant drugs such as dexamphetamine, phenmetrazine, thyroid extract. Table I shows the average two-month weight loss obtained with 'filon' and with the previous anorexiant drugs, in the different practices.

It is seen that the majority of patients (86 per cent.) lost weight while taking 'filon', and that the average weight loss for all the practices together was similar for 'filon', all the previous drugs together, and dexamphetamine

alone. Dexamphetamine was by far the most popular previous anorexiant drug used. The majority of these patients were treated with one tablet twice daily, and in those patients in whom weight loss was not satisfactory, increasing the dose to two tablets twice daily did not have much effect in increasing the weight loss. The average weight lost by new patients was exactly the same as the average weight lost by the patients previously treated with other anorexiant drugs.

Side-effects.—No side-effects occurred in 80 per cent. of the patients taking 'filon', although there were occasional instances of insomnia, vertigo, restlessness, palpitations, and other symptoms attributable to central nervous system stimulation. Five patients had to omit treatment on account of these side-effects.

CONCLUSIONS

We concluded that 'filon' (a combination of phenmatrazine theoclate and phenbutrazate hydrochloride) is a satisfactory anorexiant drug, which will produce weight reduction comparable, if not superior, to the previous forms of treatment used in this trial. With regard to side-effects, we have no comparable figures for other anorexiant drugs, but the figure of 80 per cent. of patients experiencing no side-effects at all would appear to be quite satisfactory. The twice-daily dosage is convenient for the ambulant patient, going about his everyday work, who must take an anorexiant drug over periods of several months.

The following doctors took part in this trial:—
Dr. B. Bisley, Twickenham, Middlesex
Dr. S. E. Ellison, London, N.W.6
Dr. M. Figgis, Streatham, S.W.16
Dr. H. Alan Jones, Liverpool
Dr. David Wheatley, Twickenham, Middlesex
This is Report No. 12 of the General Practitioner Research Group.

Chlorphentamine

CHLORPHENTAMINE ('lucofen') is a synthetic amphetamine derivative for which an anorexiant effect without central nervous stimulation is claimed. The preparation is in the form of 25-mg. tablets, the recommended dose at the time of this trial being one tablet thrice daily.

SCOPE OF INVESTIGATION

Seven general practitioners took part in the trial, which was designed in similar manner to the 'filon' trial. A total of 77 patients entered the trial, female patients outnumbering male patients by 4 : 1, with the maximum age incidence in the 21-40 years and 41-60 years age-groups respectively. Of these patients, 43 (56 per cent.) had been treated previously by other methods for weight reduction, and the remaining 34 (44 per cent.) had not previously been treated. As in the 'filon' trial, dexamphetamine had been

the most popular previous treatment and 80 per cent. of the patients taking this drug had lost weight, the average monthly weight loss being 4 pounds (1.8 kg.). Phenmetrazine was the next most popular previous drug and 67 per cent. of the patients taking it had lost weight, with a similar average monthly weight loss. The majority of patients in the trial were only moderately overweight, falling in the 141 to 168 pounds (64 to 76 kg.) and 169 to 196 pounds (76.7 to 89 kg.) weight groups.

RESULTS

Monthly weight losses could only be measured in 71 of the original 77 patients, since six patients omitted treatment before one month had been

	Average monthly weight loss					
	All patients			Those losing weight only		
	1st month	2nd month	3rd month	1st month	2nd month	3rd month
Dr. A	4 (14 cases)	3 (8 cases)	4 (7 cases)	4.5 (11 cases)	5 (5 cases)	5 (6 cases)
Dr. B	3 (11 cases)	1 (3 cases)	—	4 (9 cases)	4 (1 case)	—
Dr. C	6 (10 cases)	3 (5 cases)	3.5 (4 cases)	6 (10 cases)	4 (4 cases)	3.5 (4 cases)
Dr. D	4.5 (2 cases)	—	—	9 (1 case)	—	—
Dr. E	2.5 (15 cases)	1 (10 cases)	1.5 (9 cases)	4 (12 cases)	2 (7 cases)	2 (7 cases)
Dr. F	6 (11 cases)	2 (6 cases)	2 (2 cases)	6.5 (10 cases)	5 (4 cases)	2 (2 cases)
Dr. G	7 (8 cases)	6 (5 cases)	1 (3 cases)	7 (7 cases)	7 (4 cases)	2 (1 case)
Total averages	4.5 (71 cases)	2.5 (37 cases)	2 (25 cases)	5 (60 cases)	4 (25 cases)	3 (20 cases)

TABLE I.—Average weight loss (in pounds) in patients receiving chlorphentamine.

completed, owing to side-effects. Of the 71 patients remaining in the trial, 60 (84 per cent.) lost weight under treatment, this percentage varying from 50 to 100 in the different practices. The average monthly weight losses in these patients are shown in table I. It was considered that these figures compared quite favourably with those obtained with previous forms of treatment. They also illustrate the usual 'slowing-up' of effect, when anorexiant drugs are taken over a period of several months.

Various factors which might influence the results were considered, and it was found that dosage was not of importance, the dose used being satisfactory in the majority of cases. It was found, however, that previously untreated patients lost more weight (average first month's loss 6.5 pounds

[3 kg.]), as compared with the previously treated patients (average first month's loss 2.7 pounds [1.2 kg.]). This factor must always be taken into account when assessing the effects of an obesity trial such as this. It was not found that the initial degree of obesity influenced the results obtained to any degree.

Side-effects.—Of the original 77 patients, 61 per cent. experienced no side-effects at all, and in the remainder these were mainly related to the oral cavity and gastro-intestinal system. Thus, 12 per cent. of the patients complained of oral dryness and 8 per cent. complained of a bitter taste in the mouth. Nausea was complained of by 5 per cent. of patients and actual vomiting occurred in one, necessitating omission of treatment. Constipation and dizziness occurred in 5 per cent. and tiredness and headache in 4 per cent. Eight patients (10 per cent.) had to omit treatment because of side-effects, these being, in addition to the one case of vomiting: multiple (e.g. oral dryness, vertigo, nausea) in three patients; vertigo in two patients; and diarrhœa in one patient. The tablets used in this trial were uncoated, and it is understood that the product now available is in the form of enteric-coated tablets. This may reduce the incidence of this particular type of side-effect.

CONCLUSIONS

It was concluded that chlorphentamine is a satisfactory anorexiant drug, comparable in effect with dexamphetamine. Side-effects were by no means absent, but central nervous stimulation was not encountered, the main side-effects being related to the gastro-intestinal tract. Since this trial was undertaken, experimental work has shown that chlorphentamine has an exceptionally long duration of action, and it has been shown to be effective in a single morning dose of 75 mg. This fact should increase the usefulness of this form of treatment in general practice. Some patients complained of the lack of stimulant effect with chlorphentamine, since in the grossly obese patients this is often an advantage. Such patients tend to feel 'sluggish', and always feel in better health while they are taking the usual anorexiant drugs. On the other hand, other patients complain of the stimulant effect of these other drugs as exemplified by restlessness, insomnia, palpitations and 'feeling jittery'. It would seem that there is a place for both types of drug in the treatment of obesity in general practice.

The following doctors took part in this investigation:—
Dr. E. I. Boxer, Greenford, Middlesex
Dr. R. B. Chalmers, Saffron Walden, Essex
Dr. D. Craddock, South Croydon, Surrey
Dr. D. J. Davies, Swansea, Wales
Dr. J. M. Stewart, Portsmouth
Dr. J. Tees, Sydenham, London, S.E.26
Dr. David Wheatley, Twickenham, Middlesex

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A SPIRITUAL DIARIST

JOHN RUTTY, M.D. (1698-1775)

By BRIAN HILL

On April 22, 1777, Dr. Samuel Johnson wrote to his young friend, Boswell, about his plans for the coming autumn. 'I shall go to Ashbourne', he said, 'and I purpose to make Dr. Taylor invite you. If you live awhile with me at his house, we shall have much time to ourselves, and our stay will be no expense to us or him'. Without going into the question of how two extra mouths to feed could be no additional expense to their host, it is enough to say that Johnson's frugal plan succeeded. In September of that year, the two friends were happily ensconced in Dr. Taylor's house at Ashbourne. During their stay they paid a visit to nearby Derby, and returning found that 'Dr. Taylor was gone to bed. Johnson and I sat up a long time by ourselves'.

It was on this occasion that Boswell drew the Doctor's attention to an article in the current *Critical Review* on a recently published work, 'A Spiritual Diary and Soliloquies' by John Rutty, M.D.

> 'He was much diverted', he reported. 'Dr. Rutty was one of the people called Quakers, a physician of some eminence in Dublin, and the author of several works. This Diary, which was kept from 1753 to 1775, the year in which he died, and was now published in two volumes octavo, exhibited in the simplicity of his heart a minute and honest register of the state of his mind; which, though frequently laughable enough, was not more so than the history of many men would be, if recorded with equal fairness. . . . Dr. Johnson laughed heartily at this good Quietist's self-condemning minutes; particularly at his mentioning, with such a serious regret, occasional instances of "swinishness in eating, and doggedness of temper" '.

In spite of his remark that many men's lives recorded in detail would provoke readers to merriment, there is no indication that Boswell, or indeed the Great Panjandrum himself, ever contemplated for a moment the possibility that their own day-to-day doings would amuse and interest posterity. Reading Boswell's journals today we can on occasion laugh as heartily as did the Doctor and his biographer on that September evening nearly two hundred years ago.

But what was this 'Spiritual Diary' that caused them so much amusement? and what manner of man was its author?

LEYDEN AND DUBLIN

John Rutty was born in Wiltshire on December 25, 1698. The life of the child whose birth falls on Christmas Day is proverbially attended by singular good fortune, so hallowed and so gracious is the time. Outwardly Rutty's career was a successful one, but it is doubtful if he would have agreed that any special blessing followed on his date of birth. Little is known of his early life beyond the few facts that he has told us himself. As Boswell said,

his parents were members of the Society of Friends and the boy was brought up in the tenets of that sect. He himself says:—

> 'I was born among a set of more refined professors, and about my eleventh year was transplanted to a seminary of the like, being a school not only of learning but of religion; there I received a little of the heavenly fire from some of the ministers. . . . From the thirteenth to the eighteenth year of my age, I was at various mixed schools, and among aliens, and lived as without God in the world, intent all the while on my learning'.

In his early twenties Rutty was entered as a student at the University of Leyden which so many medical students of his time attended. 'Here', he says, 'the object was all nature and physic, no grace; also serious thoughts of proper qualification for a livelihood, as I had scarcely any patrimony'. The young man's studies were successful. He took his medical degree in 1723, the inaugural thesis he produced for the occasion being entitled 'de Diarrhœa'.

Returning the following year to the British Isles, he found an opening in Dublin and in that city he was to remain until his death some fifty years later. He worked hard at his profession and must have won the confidence and liking of his patients, for he gained a reputation over the years as a clever and successful physician, prepared to sacrifice his own comfort and convenience in the interests of the sick and always ready to help the poor. 'Though his medical skill was in high repute', says one account of him, 'he avoided ostentation; and his dress, address, and manner of living were consistent with the simplicity of his religious profession'. For Rutty was indeed active in his religious duties, visiting the families of Friends in the city, attending meetings regularly and, in cooperation with a schoolmaster friend, himself convening a monthly gathering of young people.

AN ACCUSING DIARY

To his patients and fellow-doctors then, John Rutty seemed an unassuming, even-tempered man of abstemious habits and kindly disposition. In his own eyes, however, he presented a very different and a much less attractive picture. Inwardly, he seems to have been tortured for years by the conviction that he was a prey to gluttony, drunkenness, bad temper and other evil habits. His daily life can rarely have been free from this obsession if we are to judge by the writings in which he recorded his struggles against his worse self.

During the last twenty years or so of his life he confided a constant stream of self-reproaches to the pages of his 'Spiritual Diary', intermingled with gloomy confessions of giving way to temptation, and only occasionally relieved by entries describing spiritually uplifting moments. Rutty was 56 years of age when he began this record (he may have destroyed earlier diaries), and he left directions in his Will for its publication after his death. No doubt he felt that it might have a beneficial effect on the minds of its readers and strengthen them in their fight against evil. Reading the Diary

today, one must admire the author's character and his devotion to his religion; equally one must share the laughter of Johnson and Boswell at his eccentricity and amusing turn of phrase. The unique flavour of the book is apparent in a selection of characteristic entries.

TYPICAL ENTRIES

Of his bouts of irritability and bad temper he records from time to time:—

'Weak and fretful. Licked spittle in two places, insolent in two others.
A frappish cholerick day.
Snappish on unseasonable calls.
Learn to repine less at small evils and flea bites, thou pitiful Jack Straw!
At my return, upon provocation, I struck my servant.
A little crabbed with two incurables.
A shocking view of myself: fierce to inferiors, viciously complaisant to superiors or equals, for the base views of profit or false honour.
Too brittle on a group of paupers. Double the guard!
Great impertinence from a patient borne tolerably, blessed be God!'.

Sloth, gluttony and drinking call for equal strictures:—

'Rose too late. O the dull body!
The first day of the week: lay late sinfully, even as others do on this day.
Lay too late in God's estimation, losing time.
Piggish at meals.
An hypochondriac obnubilation from wind and indigestion.
A little swinish at dinner.
A little incubus last night from too much spinach.
More temperance in eating vegetables, as well as more meekness, are still wanting.
Feasted beyond the holy bounds, through vicious complaisance.
This day, in God's sight, ate too much.
A vicious feast, wherein I exceeded in food and drink'.

And, on one obviously black morning-after-the-night-before, there comes a veritable *cri de coeur*:—

'Take care, take care of the fumes of cyder and whiskey, tremble at the mixture!'.

After these entries, it is something of a relief to find one that suggests that Rutty's self-admonishments did at last bear fruit. In 1770 there is a note:—

'A great change is come, and coming, viz. Instead of fierceness, meekness; instead of the spirit of drunkenness, gluttony and an inordinate attachment to books, a restraint on all these appetites'.

His 'inordinate attachment to books' and, in particular, his absorption in his researches into what he calls 'natural science', are another stumbling block:—

'Instituted an hour's retirement every evening, as a check to the inordinate study of nature.
Ten patients and eleven visits entirely absorbed my matin, to my spiritual loss.
O the ardour that still attends natural studies! Lord, lessen it!
Beware lest the physician encroach on the Christian.
A Christless day devoted to a botanic walk and an incommodious visit at a great distance'.

And at the age of sixty-four he was writing:—

'Beware of the thief, the charms of natural science!
O thou old man, who art tottering on the brink of eternity! of what use is a magazine of either fame or money (two grand idols of the people) to thee? slacken then thy pursuits after bodily science, and be no longer a fool'.

On the other hand, the Diary affords evidence of Rutty's unremitting attention to his patients, particularly those of the poorer class:—

'Eleven visits and no fee, blessed be the Lord!
Attended nine patients, six of whom were the glorious poor.
Seven patients—paupers, in Canaan's, glorious; in the world's language, pitiful'.

THE LATTER YEARS

Beyond occasional references to indigestion, there are few entries which

FIG. 1.—The Royal College of Surgeons of Ireland, St. Stephen's Green, Dublin.

mention the diarist's own health. In 1766, he records 'six weeks' confinement' owing to eye trouble:—

'An embittering dispensation of sore eyes and dull ears, the first taking me off my darling delights of reading and writing, and the second from conversation. Lord, I kiss thy rod!'

And when he was in his seventy-fourth year he had some kind of stroke, for we find an entry later:—

'Regarded the day as an anniversary of thanksgiving, being two years since my paralytic stroke; blessed years, even of sequestration from worldly cares and tempta-

tions, years of bodily weakness, yet some degree of strength returning with the fine weather, the upper region pretty clear'.

So the entries continued until the early days of December, 1774. On the 8th came Rutty's final note:—

'The voice of God now sounds louder in my great infirmity of being scarcely able to bear the cold'.

His death occurred a few months later, on April 27, 1775. Shortly before it he received a visit from a more distinguished Dissenter; this was John Wesley who, in recording it in his own journal, speaks of 'that venerable man, Dr. Rutty'. The diarist's remains found a resting place in the Quakers' burial ground in Dublin. His grave, however, has long since vanished, for the site on St. Stephen's Green is now occupied, not unfittingly, by the College of Surgeons (fig. 1). He had lived his seventy-seven years a bachelor, although there is a mysterious and intriguing reference which suggests that marriage had at least been a possibility at one time. Speaking of his early twenties, he records that there was 'some inclination to marriage, but overruled by a secret hand'.

On his death the Friends of Dublin testified that:—

'The remembrance of his useful services has endeared his memory to us and to many more. In a good old age he departed this life, with thanksgiving to God. . . .'

AN ABLE SCHOLAR

Rutty's researches into the 'natural science' which he found so absorbing and which occupied so much more of his time than he thought proper, produced a number of learned works. Soon after his arrival in Dublin in 1724, he 'opened a scheme for the improvement of the "Materia Medica" '. This work occupied some forty years of his life; it was published after his death in Latin in Rotterdam. He found time, too, for a comprehensive 'Methodical Synopsis of Mineral Waters', which listed the chief springs in the British Isles and on the Continent of Europe; and 'A History of the Rise and Progress of the People called Quakers in Ireland, 1653-1751'. Another of his interests was the study of weather conditions and their effect on health. He produced the result of his researches in 1770: 'A Chronological History of the Weather and Seasons and of the Prevailing Diseases in Dublin during the Space of 40 Years'. Finally, there may be mentioned his 'Natural History of the County of Dublin', which was published in 1772.

John Rutty was, in fact, a diligent and able scholar, just as he was a capable physician, a philanthropist and a zealous member of the Society of Friends. But, as the quaint phrasing of the introduction to his 'Spiritual Diary' puts it, 'he counted all other knowledge, comparatively, but as loss and dung' when weighed in the balance against his religious beliefs and aspirations.

CURRENT THERAPEUTICS

CLXIV.—IRON THERAPY

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THE need for iron therapy only arises when a patient is found to have an iron-deficiency anæmia—the commonest type of anæmia met with in general practice. This anæmia occurs in both sexes and at all ages, but is commonly noted in women during the childbearing age.

It develops because there is insufficient iron available for the production of the required amount of hæmoglobin. This may arise when there is: (a) an increased physiological demand for more hæmoglobin and thus iron, (b) loss of blood by hæmorrhage, and (c) an inadequate iron absorption from the alimentary tract. These situations arise following: (a) increased demands in children during the growth period, and in women during the childbearing period; (b) acute traumatic hæmorrhage, or acute or chronic, continuous or intermittent bleeding from the genito-urinary or gastro-intestinal tracts, or hæmorrhages due to abnormalities of the blood and blood vessels and disorders of blood coagulation as in hæmophilia and the purpuras; (c) nutritional deficiencies or impaired alimentary absorption of iron from the food: these may be associated with starvation, food fads and improper diets, anorexia, scurvy, pellagra, tuberculosis, idiopathic steatorrhœa and cœliac disease, sprue, ulcerative colitis, gastro-intestinal cancer, gastrectomy, gastroenterostomy. It is important to remember the common finding of achlorhydria or lowered gastric acidity in this type of anæmia.

ABSORPTION OF IRON

The correction of these iron-deficiency anæmias depends almost entirely upon supplying adequate amounts of iron in suitable form to make good the body's deficiency. Normally the necessary amounts of iron in ionic form are absorbed from the food in the alimentary tract, mostly in the duodenum. Dietary iron is usually in the form of ferric hydroxide and may be loosely combined with organic and amino-acids. Unlike the ferrous salts, ferric salts are not readily absorbed and so have to be converted to the ferrous condition in the stomach under the influence of the hydrochloric acid, organic acids and reducing agents. Various factors influence the amount of iron that is made available for absorption; in general this may be as much as 10 per cent. of the 12 to 20 mg. of ionic iron present in an average normal daily diet. Thus, these 1.2 to 2 mg. daily of ionic iron will supply the requirements of an adult male, requiring 1 to 1.5 mg. daily, but may be quite inadequate to maintain a woman's hæmoglobin level for normally she needs

more than 2 mg. daily and more than 3 mg. daily during pregnancy. The normal person is able to conserve most of the iron for very little is excreted: negligible quantities in the urine and sweat, and less than 1 mg. daily in the fæces.

The total body iron in an adult is about 3.5 to 5 g., of which about 70 per cent. is present in the hæmoglobin which is broken down when the red cells are destroyed, the hæm part of the molecule being excreted as bile pigment, whilst the iron is utilized again in the formation of new hæmoglobin, and none is excreted. Any excess amounts of iron are stored in the reticulo-endothelial cells in the bone marrow, liver, spleen and elsewhere in the form of hæmosiderin or ferritin.

Preparation	Presentation	Dosage
Ferrous sulphate	Tablets of 200 mg. of anhydrous ferrous sulphate containing 60 mg. of elemental iron	1 to 2 tablets (200 to 400 mg.) thrice daily
Ferrous gluconate	Tablets of 300 mg. of ferrous gluconate containing 35 mg. of elemental iron	1 to 3 tablets (300 to 900 mg.) thrice daily
Ferrous fumarate	Tablets of 200 mg. containing 65 mg. of elemental iron	1 to 2 tablets (200 to 400 mg.) thrice daily
Ferrous carbonate ('ferrodic')	Tablets containing 50 mg. of elemental iron and 12.5 mg. of ascorbic acid	1 to 2 tablets (50 to 100 mg. of iron) thrice daily (it is recommended by the manufacturers that these should be chewed or sucked in the mouth, but such a procedure causes staining of the teeth and is not to be recommended)
Ferrous succinate	Tablets of 150 mg. containing 35 mg. of elemental iron	1 to 3 tablets (150 to 450 mg.) thrice daily

TABLE I.—Some oral iron preparations.

The absorption of iron from the food in the alimentary tract is controlled by the needs of the body for iron, more being absorbed in the anæmic patient with low plasma iron values than in the normal individual who is not anæmic. This is thought to be controlled in the gastro-intestinal mucosal cells.

Only ferrous ions can be absorbed from the lumen of the gut into these mucosal cells, where they are oxidized to ferric hydroxide which combines with apoferritin, a protein present in the cells, to form ferritin. When all the apoferritin has been converted to ferritin in the cells, no more iron can be absorbed from the alimentary tract and there is then an equilibrium between ferrous ions and ferritin. Under the influence of a low oxygen supply, the iron in ferritin is reduced to the ferrous state again, and so can pass into the plasma, combining with the plasma iron-binding β-globulin (transferrin) after being once again oxidized to the ferric state in the presence of CO_2 in the blood.

The apoferritin thus liberated in the mucosal cells is then available to take up

more ferrous ions, while the transferrin conveys its two ferric atoms to be stored as ferritin (identical with the ferritin in the mucosal cells) and hæmosiderin. When the stores are full no more iron can be transferred by the transferrin and so none can be passed on by the mucosal cells—hence there is a 'mucosal block' control. It is this control by the 'mucosal block' that prevents absorption of excess amounts of iron when the body does not need it.

ORAL THERAPY

From this summary it will be appreciated that the correction of an iron deficiency requires the administration of a suitable iron preparation, and that if it is to be given orally then an easily ionizable ferrous salt should be the most efficient and best.

There are many ferrous salts, compounds, complexes and chelates now available for use (table I), all being claimed by their sponsors to be better, more efficient, less toxic and causing less side-reactions than any of the others, but a number of important surveys of these have shown that none of them is any better therapeutically than simple ferrous sulphate, and they are all much more expensive to use. All preparations of iron will produce some gastric irritation, nausea, vomiting, or pain in about 6 to 12 per cent. of patients, but usually not in the same individuals. With careful administration, dosage and management very few patients should have unpleasant side-effects, and when they do occur another iron preparation can be tried. There is a widespread, but fallacious, idea that iron causes constipation; this is rarely true.

Preparation	Price
	s. *d.*
Ferrous sulphate	1 6
,, gluconate	2 1½
,, amino-acetic sulphate ('plesmet')	2 3
,, fumarate ('fersamal')	2 5½
,, carbonate ('ferrodic')	2 11
,, succinate ('ferromyn')	3 3½
,, gluconate+vitamin B ('gluferrate')	5 8½
Sodium ironedetate ('sytron')	8 10
Ferrous calcium citrate ('rarical')	9 4½

TABLE II.—Approximate weekly cost to National Health Service of 210 mg. of ferrous iron daily.

It is important to remember that iron alone is adequate in these cases and should not be given with other hæmatinics or supplements, as, for example, cyanocobalamin, folic acid, liver extracts, vitamins, none of which is needed. On the other hand, they often obscure the diagnosis and response to treatment, and certainly increase the cost considerably and unnecessarily.

Ferrous salts are unstable in simple aqueous solution, becoming oxidized to the corresponding ferric salts and thus become less efficient therapeutically; consequently, they are prescribed in coated pills, tablets or capsules.

CHOICE OF PREPARATION

There is no doubt at all that the preparation of choice is ferrous sulphate in a dose of 200 to 400 mg. three times daily taken after meals; some prescribers, following the suggestion of Pierre Blaud in 1832, like to start

with one tablet a day, gradually increasing it to the full dose, thus avoiding possible gastric discomfort in sensitive patients. Exsiccated ferrous sulphate contains a high proportion of elemental iron, is absorbed easily and efficiently, and is still easily the cheapest form of iron therapy (table II). In patients with achlorhydria, the taking of a hydrochloric-acid-pepsin drink after meals, together with 50 mg. of ascorbic acid, enhances the efficiency with which the ferrous iron is absorbed. Very occasionally, a patient may not tolerate ferrous sulphate and in such a case ferrous gluconate or fumarate may be tried instead. When one considers the efficient response following the use of ferrous sulphate and its cheapness, there should be no need at all to use other more expensive (some much more expensive) preparations (see table I and II).

With effective oral treatment the hæmoglobin should rise by about 1 per cent. per day but it is important that treatment be maintained regularly until the hæmoglobin has risen to a normal value; long before this the patient will feel very much better and show a striking improvement in her general condition and colour. As previously indicated, owing to the control of iron absorption into the mucosal cells, in the early stages of treatment much more iron is absorbed when given orally and so a smaller dose of ferrous sulphate may be needed, but later, when the hæmoglobin reaches about 75 to 80 per cent. (11 to 11.7 g.) absorption of iron is slowed down by the 'mucosal block' and it may be necessary at this point to increase the dose for a time. Even when the hæmoglobin has returned to a normal level, it is wise to continue on a small dose of iron until the iron stores have been fully replenished. Sometimes, in children and in elderly patients, especially those with gastric lesions, tablet therapy may not be suitable and then a liquid preparation is desirable. In these cases excellent results can be obtained using a colloidal ferric hydroxide preparation such as 'neoferrum' in doses of 1 to 2 teaspoonfuls (4 to 8 ml.) three times daily, which causes neither gastric irritation nor constipation; in fact many patients find it slightly and desirably relaxing.

The orally administered iron preparations are undoubtedly the first method of treatment of patients with iron-deficient hypochromic anæmia. The speed of response to oral therapy in uncomplicated cases is nearly as quick as that obtained using intravenous iron therapy, whilst intramuscular iron therapy is less rapid.

FAILURE TO RESPOND

Failure to respond may be noted occasionally in some patients and in these 'refractory' patients it is important to look for the reason, bearing in mind that the urgency is to discover the cause rather than to try some other form of treatment. This refractoriness may be due to:

(a) An incorrect diagnosis; the hæmatological situation should therefore be reviewed carefully.

(b) The patient may not be taking the tablets regularly or in the proper dosage.
(c) The iron preparation may not be absorbed in the alimentary tract due to conditions such as gastritis, gastroenteritis, chronic diarrhœa, steatorrhœa, sprue, cœliac disease, tuberculosis or cancer of the gastro-intestinal tract.
(d) Chronic or acute persisting hæmorrhage—usually in the alimentary tract, as may be seen in association with bleeding duodenal ulcer, purpura, or a bleeding diathesis.
(e) Complicating conditions such as gross infection, renal disease, hepatic cirrhosis, chronic arthritis, malignant disease especially with metastases.

TOXIC EFFECTS DUE TO IRON POISONING

Accidental poisoning, nearly always in children, after taking large doses of iron tablets has increased in frequency during the last decade and ferrous sulphate is said to be second only to aspirin in this respect. The greatly increased use, especially by pregnant mothers, of coloured, sugar-coated iron tablets resembling sweets, which are left within the reach of children, calls for a firm warning when this form of therapy is being used in a family where there are young children. Rarely does one know how many tablets have been taken but massive doses have led to a 50 per cent. mortality.

The symptoms are those of severe gastro-intestinal irritation, shock, hæmatemesis, tachycardia, pallor or cyanosis, drowsiness, coma, and cardiovascular collapse; later, a strong corrosive action on the gastric mucosa may result in the production of a pyloric stenosis.

Immediate treatment is called for and can save life. Vomiting should be induced, if possible after a milk drink, and followed by gastric lavage with 1 per cent. sodium bicarbonate, and immediate removal to hospital. Treatment of shock requires warmth, oxygen therapy, and intravenous fluids, whilst the gastric irritation can be soothed by 1 per cent. sodium bicarbonate, and aluminium hydroxide or bismuth carbonate. The administration of 500 mg. of calcium disodium edathamil (EDTA) in isotonic glucose-saline intravenously slowly over six to twelve hours, to reduce the serum iron levels, may be of great value. Subsequently, the child must be kept under observation because of the risk of pyloric obstruction developing.

PARENTERAL IRON THERAPY

Suitable iron preparations can be given intravenously or intramuscularly to patients: (a) who will not or cannot take oral iron therapy, (b) in whom iron is not absorbed for some reason from the gastro-intestinal tract, (c) to whom oral iron preparations cannot be given on account of gastro-intestinal lesions such as severe ulcerative colitis, Crohn's disease, or (d) when there is continuing severe blood loss. Sometimes there is a need for a quicker response to iron therapy than can be obtained by the oral route, such as a severe hypochromic anæmia found during the later stages of pregnancy, or in preparation for an operation. In such circumstances an intravenously administered iron preparation is indicated if blood transfusions are not desired.

INTRAVENOUS THERAPY

By intravenous iron therapy, using the saccharated iron preparation 'neoferrum (intravenous)', the calculated required dose of iron can be given, if the veins are satisfactory, with the knowledge that the expected result will take place. Bedridden and emaciated patients can also be more easily treated than by using oral or intramuscular iron preparations.

The total iron dosage of 'neoferrum (intravenous)' required can be calculated on the basis of 25 mg. of elemental iron for each 1 per cent. deficit of hæmoglobin (Haldane); thus, a patient with 60 per cent. hæmoglobin would require (100 – 60) × 25 mg. of iron = 1000 mg., to which must be added a 50 per cent. supplement for the body iron stores. Another method in adults is to give 50 mg. of elemental iron for each 1 per cent. deficit of hæmoglobin: this gives a slightly higher dosage, allowing a greater amount for body reserves.

Method of administration.—The injection is given into an antecubital vein, beginning with doses of 1 ml., 2 ml., 5 ml., 7.5 ml., and 10 ml., respectively on each succeeding day, then continuing with 10 ml. daily or 10 ml. twice

Preparation	Cost
	s. *d.*
Intravenous	
'Neoferrum (intravenous)'	17 11½
Intramuscular	
'Imferon'	29 5

TABLE III.—Cost to National Health Service of 1000 mg. of iron given parenterally.

daily until the total dosage has been given. 'Neoferrum (intravenous)' is supplied in sterile ampoules containing 100 mg. of elemental iron in 5 ml.

The dose to be given is taken up into a 20-ml. syringe, the needle is then changed to avoid contaminating the tissues around the vein with any 'neoferrum' adherent to the outside of the filling needle, and then inserted into the vein; about 10 ml. of blood are withdrawn into the syringe to mix with the 'neoferrum (intravenous)' there, and then the whole is reinjected slowly at an approximate rate of 1 ml. per 15-20 seconds.

It is important to prevent leakage outside the vein, which would cause local pain and inflammation of the surrounding soft tissues.

If this technique is followed carefully, no generalized reactions should occur at all but occasionally a patient may have slight flushing, palpitation, slight temporary tightness in the chest, or slight lumbar backache. If these occur it is always at the end of the first two or three injections only, but tolerance develops and later doses can usually be given without these recurring.

Excellent results are obtained using this preparation of 'neoferrum (intravenous)' and the hæmoglobin rises rapidly at a rate of more than 1 per cent. daily to normal levels without need of further iron, and this improvement persists. It is essential, of course, to have a good intravenous

technique. It is much cheaper than the intramuscular preparations (table III).

INTRAMUSCULAR THERAPY

Iron preparations for intramuscular administration differ from those for intravenous use in that they are complexes of ferric hydroxide and low-molecular-weight iron-dextran. Such a preparation is 'imferon', which is put up in ampoules of 2 ml. and 5 ml. of a sterile solution containing 50 mg. of elemental iron per ml.

Technique.—With the patient lying on one side, the injection is given by deep insertion into the outer and upper quadrant of the buttock; it is necessary to use a long (2.5-inch [6 cm.]) intramuscular needle for this purpose, which is attached to the syringe after it has been filled from the ampoule, using another needle so that no trace of the solution is on the outside of the needle used for the injection; this diminishes pain and brown staining in the superficial tissues.

With the thumb of the free hand the skin is drawn to one side, the needle is then inserted deeply and the injection given slowly; when the needle is withdrawn, the released skin moves back into its original place thus forming a zig-zag needle track which prevents leaking back of the 'imferon' and again helps to reduce the degree of skin staining.

The initial dosage of 'imferon' employed is 1 ml. (50 mg.), increasing on subsequent days to 100 mg. (2 ml.) or 150 mg. (3 ml.); in some cases the dose may be increased to 250 mg. (5 ml.) but there is then a much greater likelihood of local pain occurring. Following this course of intramuscular iron therapy the hæmoglobin will usually rise progressively to normal levels but at a slightly slower rate than is seen after intravenous administration of 'neoferrum (intravenous)'.

Such preparations of iron for intramuscular use are easier to administer than the intravenous preparations, especially when veins are poor as in obese patients, the patient may suffer varying degrees of pain at the site of injections afterwards, lasting for a week or more, whilst the inguinal glands may become moderately enlarged and tender. Brown staining of the skin is commonly seen to a varying degree, particularly after a full course of injections of 'imferon' has been given. General symptoms, although not common, have been recorded, such as dyspnœa, tight feelings in the chest, backache, tachycardia, anxiety, urticaria, flushing, transient giddiness and headaches.

CONCLUSION

Finally it should again be emphasized that only iron-deficiency anæmias can be expected to respond to iron therapy, and that the intramuscular and intravenous injection of iron compounds is only called for in those infrequent patients in whom oral iron therapy has failed to produce satisfactory results.

CALLING THE LABORATORY

XX.—FUNGUS INFECTIONS

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THESE are most conveniently considered under the three headings of keratin, subcutaneous infections and pulmonary infections.

KERATIN INFECTIONS

Disease	*Organism*
Superficial mycoses	
(i) *Skin:*	
Erythrasma	*Nocardia minutissima* (B)
Pityriasis versicolor	*Malassezia furfur* (Y-L)
Moniliasis	*Candida albicans* (Y-L)
Otomycosis	*Aspergillus niger* (F)
(ii) *Hair:*	
Trichonocardiosis axillaris	*Nocardia tenuis* (B)
Piedra	*Piedraia* and *Trichosporon* species (F)
Ringworm	
Tinea of skin and of hair and nails (see table I)	*Microsporum* species (F) *Trichophyton* species (F) *Epidermophyton* species (F)

(B = Bacterium; Y-L = Yeast-like fungus; F = Filamentous fungus)

Erythrasma.—Reddish-brown macular eruptions sometimes showing slight desquamation, and almost entirely limited to the axillary and genito-crural regions, suggest this diagnosis. Nails and hair are not involved. After wiping the affected area with a swab soaked in acetone or ether, the zone is scraped with a blunt scalpel, collecting the scrapings on a clean piece of paper. This is folded to make a small sealed package for despatch to the laboratory. The causative organism has not been cultured, so that the finding of delicate filaments of bacterial dimensions is used for confirmation of the diagnosis.

Pityriasis versicolor.—In this disease, brownish-red slightly desquamating macules mainly involve the trunk; the extremities are rarely affected. Pseudoachromia of affected areas may follow exposure to sunlight. Nails and hair are not involved. The method of examination is as for erythrasma. The causative fungus has not been cultured, and the finding of clusters of round budding yeasts together with wavy threads of mycelium provides the necessary confirmatory evidence. The mycelium readily fragments into short lengths during examination. Skin scales are examined in 10 per cent. potassium hydroxide or by staining with methylene blue after defatting.

Moniliasis.—This infection is simulated quite often by other conditions, such as bacterial infections and maceration due to hyperidrosis. The skin, particularly of intertriginous zones, the paronychial tissues and mucosæ of mouth and genitalia are frequently involved. Rarely nails become infected. Characteristic of skin infections are well-marginated, bright-red, exuding areas with borders consisting of white macerated keratin. Surrounding these lesions vesico-pustules are found. Mucous membrane infection results in

intense erythema and white plaques of exudate; lesser degrees of inflammation may be associated with pruritus and discharge. When moniliasis is considered to be a possibility, the existence of predisposing factors must be investigated. Skin maceration such as arises in obesity and frequent immersion in water, the presence of diabetes mellitus and the prolonged use of broad-spectrum antibiotics are among such factors. The causative fungus is characterized by thin-walled budding yeast cells often developing short filamentous structures which also exhibit budding at points of constriction.

Skin scrapings are taken as previously described, and whenever possible a swab moistened with broth is rubbed over the affected area for culture. Swabs are also taken from zones of possible mucosal infection, detaching any plaques of exudate. Skin scrapings may be satisfactorily examined after periods of delay but swabs and exudates must be cultured promptly. If there is delay of more than a few hours, the yeasts may proliferate at room temperature and give a false impression of the degree of infection. Approximately one-third to one-half of the population harbour *Candida albicans* as part of the normal flora. The yeast is identified as distinct from other *Candida* species by sugar fermentation reactions and its ability to form characteristic spores on special media. Skin and serological tests are of no help.

Otomycosis.—This type of subacute or chronic external otitis is due to *Aspergillus niger* and possibly other *Aspergillus* species. The fungus is present in the sleeve of exudate obstructing the meatus. Part of the exudate should be removed for direct examination and also material taken with swabs moistened in broth for culture. It is necessary that fungus mycelium and sporing structures be seen on direct examination of the exudate since the fungi concerned are common contaminants, ubiquitous in the atmosphere. Positive cultures alone are of no significance.

Trichonocardiosis axillaris.—Waxy nodules, usually of yellowish colour, affect the shafts of axillary hairs in this condition; rarely, pubic hairs are colonized. Some types of infection are associated with additional organisms producing red or black pigments which stain the clothing. For laboratory investigation, shaved hairs are sent in paper packages. The causative organism has not been cultured and the finding of irregular nodules containing embedded delicate filaments of bacterial dimensions is diagnostic.

Piedra.—This is a subtropical infection only occasionally seen in Europe. Compared with the preceding condition, nodules are hard and more discrete. Direct examination in 10 per cent. potassium hydroxide shows fungus filaments and cultures yield specific fungi.

Ringworm.—Three main types of ringworm organisms invade the skin, whilst certain species also attack to greater or lesser degree hair and nail (table 1). The division of fungus filaments to form spores in and around hair shafts provides valuable suggestive evidence as to the causative organism concerned. Further valuable information is provided if fluorescing material is produced in hair as seen under Wood's ultra-violet light.

Skin scrapings from hyperkeratotic areas and the roofs of vesicles are

placed in paper packages for laboratory examination. Hair stumps, or any long fluorescing hairs, are removed. When fracture has occurred at scalp level, intrafollicular portions of the shaft should be extracted for examination with a Hagedorn needle. In the case of nails, the whole thickness of any hypertrophied or crumbling areas is clipped off. It is important that plenty

Fungus	Hair invasion			Nail invasion
	Degree	Spore arrangement	Fluorescence (Wood's light)	Degree
Microsporum:				
M. audouini (M)	++	SSE	++	—
M. canis (A)	++	SSE	++	—
M. gypseum (S)	+	SSE	—	—
Trichophyton:				
T. mentagrophytes (A)	+	SSE	—	+
T. mentagrophytes var. interdigitale (M)	—	—	—	+
T. rubrum (M)	—	—	—	+++
T. verrucosum (A)	+	LSE	—	—
T. sulphureum (M)	++	E	—	+
T. violaceum (M)	++	E	—	+
T. schœnleini (M)	++	E	+	+
Epidermophyton:				
E. floccosum (M)	—	—	—	±

Natural habitat of fungus:—M=Fungus infects man only; A=Fungus infects various animals which transmit infection to man; S=Fungus present in soil; infects man and animals.
Type of hair infection:—SSE=Small-spored ectothrix; LSE=Large-spored ectothrix; E=Endothrix.

TABLE I.—Susceptibility of hair and nail to infection by ringworm fungi which infect skin.

of material be obtained for mycological examination. The identification by the laboratory of fungus filaments and spores of ringworm type is valuable evidence of disease which may be confirmed by culture. The material is first examined microscopically after adequate maceration in 10 to 30 per cent, potassium hydroxide. Identification of the ringworm species involved provides information about prognosis and origin of infection. Cultures are carried out by inoculating fragments of keratinous material on appropriate nutrient medium. Skin and serological tests are not of any real value for diagnosis.

SUBCUTANEOUS INFECTIONS

Disease	*Organism*
Actinomycosis	*Actinomyces israeli* (B)
Actinomycetoma	*Streptomyces* species (B)
Maduromycetoma	*Madurella* species, etc. (F)
Chromoblastomycosis	*Phialophora* species (F)
Sporotrichosis	*Sporotrichum schencki* (D)

(B=Bacterium; F=Filamentous fungus; D=Dimorphic fungus)

These are rare infections in Britain. They result from the introduction of the causative organism into the subcutaneous tissues as a result of trauma.

Actinomycosis and actinomycetoma are investigated by bacteriological techniques, and maduromycetoma, chromoblastomycosis and sporotrichosis by appropriate culture investigation using mycological media. When subcutaneous granulomas have already ulcerated, swabs of exudate,

pus and any 'grains' in the discharge are required for culture. Smears on clean glass slides should also be made. Ideally, a biopsy of any non-ulcerated lesion is taken using sterile precautions. One-half of the material is placed in a dry sterile container for culture and animal inoculation, and the other half in 10 per cent. formol-saline for histological examination. Unique among these infections is the lymphatic spread which occurs in sporotrichosis. This disease is caused by a dimorphic fungus, by which is meant an organism existing in nature in the filamentous form but which becomes converted to a yeast or other unicellular structure on entering the tissues. There are no valuable skin or serological tests in these infections.

PULMONARY INFECTIONS

Disease	*Organism*
Endogenously acquired	
Actinomycosis	*Actinomyces israeli* (B)
Moniliasis	*Candida albicans* (Y-L)
Exogenously acquired	
Primary infections:	
Torulosis	*Cryptococcus neoformans* (Y)
Histoplasmosis	*Histoplasma capsulatum* (D)
Coccidioidomycosis	*Coccidioides immitis* (D)
Blastomycosis	*Blastomyces dermatitidis* (D)
Secondary infections:	
Aspergillosis	*Aspergillus fumigatus* (F)
Mucormycosis	*Rhizopus* species (F)

(B = Bacterium; Y = Yeast; Y-L = Yeast-like fungus; F = Filamentous fungus; D = Dimorphic fungus)

Endogenously acquired infections are caused by organisms which are inhabitants of the upper respiratory tract.

Actinomycosis is characterized by the presence of typical 'granules' in sputum or pus. Any such material requires immediate laboratory examination by microscopy and culture. In the absence of granules, the mere finding of *Actinomyces israeli* may be misleading, since the organism may vegetate in tonsillar crypts or carious teeth.

Moniliasis.—Bronchial infection by this organism is rarely of significance. *Candida albicans* is scantily present as a normal inhabitant of the upper respiratory tract, so that when it is isolated from the sputum it is important that a quantitative assessment be made. Large amounts of fungus may be present when prolonged antibiotic therapy has been used in bacterial infections. When membrane is expectorated some of this should be examined.

Exogenously acquired infections are caused by the inhalation of fungus cells present in dust.

Torulosis.—This condition has most commonly been confused with neoplasm of the lung, and, when disseminated disease develops, with meningeal tuberculosis. Both in sputum and in cerebrospinal fluid, the causative fungus is seen as budding yeast cells surrounded by wide mucoid capsules. The demonstration of the yeast is practically pathognomonic of disease and confirmation is by culture and animal inoculation. Skin tests and serological examinations serve no useful purpose in diagnosis.

Histoplasmosis, coccidioidomycosis and blastomycosis are three pulmonary infections which are usually benign but which may occasionally disseminate to involve the meninges, skeletal system and skin. They are caused by the inhalation of airborne spores of dimorphic fungi. The diseases have a distinctive world distribution which has been mapped out by skin-testing surveys. Antigens for such tests are valuable for diagnosis and are known as histoplasmin, coccidioidin and blastomycin. Tests are carried out and read as for the Mantoux reaction. Furthermore, serology plays a useful part both in diagnosis and in assessing prognosis. The diseases have been met with in greater numbers in Europe as a result of increasing world travel. Histoplasmosis is the most widely distributed of them, coccidioidomycosis and blastomycosis being largely limited to North America. The diseases may mimic a number of pulmonary conditions, particularly tuberculosis. The most characteristic of the pulmonary lesions are the discrete calcified miliary lesions of histoplasmosis, and the thin-walled single residual cavities of coccidioidomycosis. As in tuberculosis, careful examination of sputum both microscopically and by culture is necessary; the finding of the significant mycelial and yeast phases is pathognomonic of disease.

Aspergillosis.—This infection, which is being seen with increasing frequency in Europe, exists in two forms. In the *saprophytic type*, the fungus grows profusely in damaged bronchial or lung tissue. It may invade areas of unresolved pneumonia, lung abscess, zones of infarction and healing tuberculous cavities. A compact mass of fungous mycelium ultimately develops which produces an aspergillus 'mycetoma'. Radiologically this is seen as a spherical opacity capped by a thin crescent of translucency. Hæmoptysis is an important symptom. The *allergic type* is seen in patients with a history of asthma and in whom episodes of pulmonary collapse and consolidation become the sequelæ of repeated bronchial obstructions. Such blockages result from the accumulation of tenacious exudate consisting of mucus, fibrin and eosinophils. By laboratory examination it is possible to demonstrate *Aspergillus* mycelium in this material. Cytological examination both of sputum and of peripheral blood shows the presence of eosinophilia.

In the diagnosis of broncho-pulmonary aspergillosis, repeated culture examinations of freshly expectorated sputum for the presence of *Aspergillus fumigatus* are necessary. A single isolation of the fungus may be of no significance since the organism is a frequent airborne contaminant. In the allergic type of disease, skin tests using *Aspergillus* antigen, if positive, provide additional evidence of infection. Serological tests to demonstrate the presence of precipitins are more valuable in both types of disease. Occasionally, and particularly in cases of leukæmia and Hodgkin's disease, dissemination of *Aspergillus* infection occurs.

Mucormycosis is a pulmonary infection caused by a ubiquitous fungus. Infection tends to complicate diabetes mellitus, leukæmia and other debilitating diseases. Cultural examination of freshly expectorated sputum is required.

PRINCIPLES OF REHABILITATION

VIII.—DOMESTIC INDEPENDENCE

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Whereas personal independence aims at making a person less of a liability, domestic independence should aim at turning the handicapped individual into an asset. Certain advantages of this are obvious but one advantage not always appreciated is that the more useful a handicapped person is in the home, the more secure is her position.

THE KITCHEN

If one is fortunate enough to come in at the start when suitable accommodation is being planned for a handicapped person, a great opportunity occurs for designing the kitchen layout from scratch. In these circumstances it is most important to pay attention to:—

(i) The position of the doors; this will include back door, kitchen and larder doors.
(ii) The position of the sink, cooking stove, and preparation table.

The ideal arrangement may well consist of a U-shaped kitchen (fig. 1) with the stove at one end; the sink in the middle, and the preparation table at the other end. The doors should be sited at the ends of the 'U'.

The next important general consideration is that of heights and levels. Ideally, the three items mentioned above should have their tops all on the same level (it is a great help to be able to slide the big saucepans of potatoes from the preparation table via the sink, on to the stove, without having to lift them, and return the similar way to the sink for draining off the water on completion of cooking). The actual working height should be that which is most easily managed by the patient, who may be seated either in a wheel chair or in a swivel type office chair (fig. 1) so that she can reach all parts of the kitchen without standing up.

When choosing the stove, certain ones can be split into separate components of oven and burners or hot plates, and the oven portion may be raised on a small plinth with advantage.

With regard to the sink, an important point is to get a shallow six-inch (15 cm.) sink in preference to the normal eleven-inch (28 cm.) sink, since this allows the knees to go under the sink and the arms to assume a natural position when working in the sink. It will also be a help if the swivel type hot and cold fitment is set slightly down one side of the sink so that the nozzle can swivel over the draining board on which kettles or saucepans can be stood while filling.

The question of drawers and shelves for equipment must now be considered. A usual arrangement is a series of shallow drawers under the

FIG. 1.—'U'-shaped kitchen.

FIG. 2.—Screw-topped jars with the lids screwed under the shelf, being easily undone by a one-handed patient.

FIG. 3.—The farther-away hemiplegic patient is peeling a potato which is impaled on the board on four nails. In the foreground are shown the one-handed pastry roller; the ply-wood board which accommodates the pudding and pastry basins; the gadget for blending fats and sugar; and the obliquely placed swivelling sink tap.

preparation table. These should be of sufficient depth to hold only one layer of implements. Shelves for saucepans, jars, and the like should be a convenient height above the working level, and this should be sufficient to allow the tallest object in use to stand upright — usually the bottle of cordial. These shelves can, with advantage, be made very wide so that they extend out much farther than normal, thereby bringing the articles upon them much nearer the reach of a patient in the sitting position. Figure 1 illustrates a 'U'-shaped kitchen layout with semi-circular shelves, built on a decreasing radius as they go upwards, so that the front edge of them remains more or less on a constant radius from the patient's shoulder. Underneath these shelves are screwed the lids of screw-type jars; these not only act as useful containers, but are easily undone by one-handed people (fig. 2).

FIG. 4.—An ordinary cheese grater adapted for one-handed use; leaning up against the wall to the left can be seen the potato peeler board with its three nails.

FIG. 5.—A hemiplegic housewife with a flaccid right upper extremity using the modified tea tray, partly as a tea-trolley and partly as a walking aid.

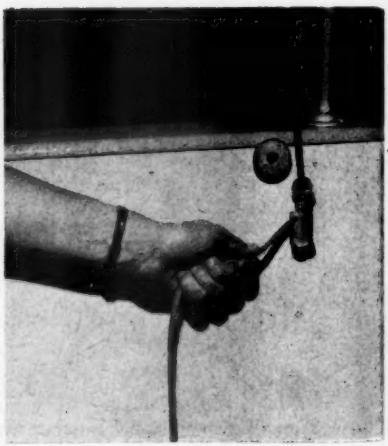

FIG. 6.—The dinghy type jamming cleat being used for hauling up the airer.

Unfortunately, it is seldom feasible to arrange kitchens in these ideal circumstances. When dealing with an old existing kitchen, the aim should be to place the stove, preparation table and sink as near together as possible, and this can often be done in a right-angled corner of the kitchen. It is usually much easier to move the gas stove, calor gas stove or electrical stove than to move the sink. As a temporary measure, considerable help can be

FIG. 7.—The hopper attachment to the ordinary mangle.

afforded by arranging short lengths of board to connect up stove, sink, preparation table and the like, thereby enabling the patient to slide utensils along instead of lifting and carrying.

The main activities performed in the kitchen can be summarized as follows: (i) Cleaning and preparation of food, (ii) washing-up, (iii) food transport, (iv) laundry. The main disabilities to be helped will be: (a) Poor locomotion, (b) poor grip, (c) one-handedness. Different combinations of these disabilities may occur in the main disability-producing diseases: e.g. hemiplegia, polio, multiple sclerosis, rheumatoid arthritis and osteo-arthritis, trauma and old age.

FOOD PREPARATION

Food preparation involves holding the object for cutting, cleaning, peeling or grating, and in the case of pastries will involve sifting and mixing. Holding of the object can be carried out in many cases by a simple board with three or four nails driven through from the under-side and suitably spaced (fig. 3, 4). Most potato peelers now can be bought with a blade suitable either for left- or right-hand use. This, like the majority of items, can be purchased at the ordinary ironmonger. When grip is poor, handles of items can be thickened by rubber bicycle grips as described in previous articles. When the patient has only one useful hand, the following items are especially useful (fig. 3): wide type of fish slice; an Archimedes type of egg

whisk; cheese grater, lodged three inches (8 cm.) up on a slotted block of wood above the working surface, under which a plate can be slid (fig. 4). The ordinary domestic paint roller in which the lambswool roller has been replaced by a wooden roller, serves as a one-handed rolling pin. The very simple arrangement of half-a-dozen semi-circular strong steel wires for blending fats and sugar, and finally a sliding half-inch (1.25 cm.) three-ply

FIG. 8.—The 'Bylock' type of iron in its tipped back position, away from the fabrics and ironing board.

board housed under the preparation table, and having two or three holes of different diameter, in which pudding and pastry basins can be held in position, completes the list. The method of using these everyday items requires no special comment.

Food having been prepared, it will then be necessary to transport it to where it is to be eaten, and the handicapped housewife finds the modified tea-trolley (fig. 5)—having the top shelf level with the preparation table, and with dimensions of 20 x 20 inches (50 x 50 cm.)—very useful. This modified tea-trolley differs from the standard model and facilitates the loading and increases manœuvrability.

LAUNDRY

The other activity dealt with in the kitchen is laundry. In the past we have usually recommended that this be sent out, because of the difficulty of a handicapped person hanging articles out on the line. Now it is possible to get articles much dryer than previously owing to the improvement in mangles and the advent of the high-speed spin dryer, and most items can now be dried in the kitchen by means of an ordinary overhead clothes airer drawn up to the ceiling by ropes and pulleys. Hauling this up is much

facilitated in the case of the one-handed by using the jamming cleat which is normally used for the centre boards of dinghies (fig. 6). When mangling has to be done as a single-handed operation, it is important to fit the mangle on to a hopper on to which the clothes can be placed so as to provide a continuous feed to the mangle rollers (fig. 7).

AN ALL-ELECTRIC KITCHEN

The gadgets and methods mentioned above are normally quite adequate for practically every variety of patient capable of rehabilitation. Recently, however, we have designed a kitchen in which everything possible is electric. This includes the 'Kenwood' food mixer, knife sharpener, and 'wastemaster'. This latter eliminates most of the routine trips to the dustbin. In addition, we have installed in lieu of a larder, the combined large capacity refrigerator and deep freeze, and finally, the 'Bylock' type of electric iron. This is what might be termed a 'self-righting' iron which is heated and thermostatically controlled in a normal manner, but when not held in the hand, is so balanced that the hot shoe tips up in the air and so is not in contact with any part of the material or ironing board (fig. 8).

REVISION CORNER

HÆMOGLOBINURIA

THE excretion of free hæmoglobin through the kidney is not a disease process but is a symptom (or sign) of rapid intravascular breakdown of red cells.

RECOGNITION

The appearance of the urine is determined by two factors: the concentration of hæmoglobin, which is proportional to the rate and quantity of hæmolysis, and the amount of methæmoglobin present. In an acid urine red or pink hæmoglobin tends to be converted to the dark-brown methæmoglobin. The colour of urine containing free hæmoglobin may therefore range from near normal through pink to red or through brown to black. Since leucocytes and epithelial cells are rarely present in hæmoglobinuria and red cells are, by definition, absent, in most cases the urine will be clear, translucent and without deposit. In the individual patient the degree of discoloration may vary from specimen to specimen and, particularly when the episode of hæmolysis has been transitory, only the first of subsequent urinary samples may be abnormal.

TESTS

In a number of conditions, some of which will be considered later, the presence of other pigments in the urine may suggest hæmoglobinuria. In

practice the tests for hæmoglobinuria are so simple and easily applied that it is reasonable, as a first step in the examination of such urines, to establish or exclude free hæmoglobin or methæmoglobin as the cause.

(a) *Ortho-toluidine type of test.*—In practice, commercially produced tablet tests based on an ortho-toluidine reaction will be found more satisfactory than the benzidine or guaiac tests. With these preparations (e.g. 'occultest', 'hæmatest') hæmoglobin in urine may be detected in concentrations which will not produce any macroscopic colour change in the urine. These tests are reasonably specific for hæmoglobin and will give, for example, negative results in porphyrinuria. False-positive reactions may occur if the patient is receiving iodides or has pyuria. If pus is present the urine should therefore be boiled and cooled before testing to inactivate leucocyte peroxidases. These tests will not, of course, discriminate between intracorpuscular hæmoglobin (hæmaturia) and hæmoglobinuria which must be distinguished by microscopic examination of a centrifuged deposit for red cells.

(b) *Spectroscopic examination.*—Hæmoglobin can be identified by its characteristic absorption bands. In practice, if the ortho-toluidine test is positive, this is sufficiently specific and sufficiently sensitive to make spectroscopy an unnecessary elaboration. If the test is negative some alternative explanation of the urinary pigmentation should be considered.

DIFFERENTIAL DIAGNOSIS

In a number of situations the appearances of the urine may suggest hæmoglobinuria.

(a) *Hæmaturia.*—In this condition, although the ortho-toluidine test will be positive, the intact red cells make the urine 'smoky', form a recognizable deposit, or can be identified microscopically. Although protein and various casts may be present in both hæmaturia and hæmoglobinuria, intact red cells are not found in the urine following intravascular hæmolysis. In doubtful cases rapid examination of the centrifuged deposit from a fresh sample is essential, for hæmolysis of red cells in urines of low specific gravity may suggest hæmoglobinuria rather than hæmaturia.

(b) *Drugs, dyes and foods.*—Pinkish-red urine containing neither hæmoglobin nor red cells, may be passed in the early stages of phenindione treatment. This may surprise the patient and frighten the doctor but has no other significance and is usually transitory. Similar disturbances may follow consumption of beetroot, coloured boiled sweets or laxatives containing phenolphthalein. Hæmoglobinuria may be excluded by the tests already described.

(c) *Porphyrinuria and porphyria.*—In these conditions the urine may appear normal, pink, reddish or reddish-brown. Although acute porphyria is very uncommon it is worth considering in patients in whom, for example, unusual colouring of the urine is associated with unexplained abdominal or neurological symptoms. In such cases the ortho-toluidine test will be

negative. In fresh urine, a reddish-purple colour may be observed with Ehrlich's aldehyde reagent if porphobilinogen is present and this, unlike that produced when urobilinogen is present, will be insoluble in chloroform. For further investigation special laboratory facilities are required.

(d) *Myoglobinuria.*—Myoglobin may appear in the urine following severe muscle trauma or disease. It does not produce any tinting of the plasma but otherwise can only be distinguished from hæmoglobin by reversion spectroscopy.

MECHANISM

Following intravascular hæmolysis there is a rise in plasma hæmoglobin. With values of less than 40 mg./100 ml. no macroscopic change is observed in the plasma but above this level the plasma will appear pink or red. Only with concentrations of plasma hæmoglobin greater than 100 to 140 mg./100 ml. will free hæmoglobin appear in the urine and until recently it was thought that this value was the renal threshold for hæmoglobin. It appears, however, that hæmoglobin, liberated in the plasma, is immediately bound to a specific globulin (hapto-globin). This complex is not excreted by the kidney and only when the hapto-globin is saturated by considerable rapid hæmolysis is any excess hæmoglobin free in the plasma and excreted in the urine.

CAUSES

Once the fact of hæmoglobinuria is established it may be assumed that there has been rapid and fairly considerable intravascular hæmolysis. In certain hæmolytic anæmias, congenital spherocytic anæmia for example, red cells are broken down in extravascular reticulo-endothelial sites such as the spleen, and even acute hæmolytic episodes do not produce hæmoglobinuria. Some of the less uncommon causes of intravascular hæmolysis which may produce hæmoglobinuria are:—

Incompatible blood transfusion
Drugs (e.g. sulphones, sulphonamides, PAS, quinine, quinidine, mephenesin)
Chemical agents (e.g. lead, naphthalene [moth-balls], benzene)
Idiopathic acquired hæmolytic anæmia
Malaria

Among the less common conditions in which hæmoglobinuria may occur are:—

Paroxysmal nocturnal hæmoglobinuria
Paroxysmal cold hæmoglobinuria
March hæmoglobinuria
Favism
Following burns

MANAGEMENT

Whilst the clinical history and findings may suggest a diagnosis, this may ultimately depend on laboratory demonstration of sometimes transient abnormalities in blood and urine. Specimens of urine and samples of clotted and unclotted (sequestrene or oxalate) blood should therefore be obtained as soon as it is established that the patient has hæmoglobinuria.

It is doubtful whether the excretion of free hæmoglobin through the

kidney has, by itself, any temporary or permanent effect on renal function. The partial or complete renal failure which may follow an incompatible blood transfusion, for example, is predominantly the result of reduced renal blood flow and the contribution of the hæmoglobinuria is probably negligible. The management of hæmoglobinuria is therefore the management of the condition causing it.

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INSULIN HYPOGLYCÆMIA

THE normal fasting blood-sugar level lies between 60 and 100 mg. per 100 ml. Most methods of blood-sugar determination in the past have measured total reducing substances; if true glucose is measured the figure is usually about 10 to 20 mg. lower.

CAUSATION

Symptoms of hypoglycæmia develop at different levels of blood sugar in different patients, varying from about 30 to 60 mg. per 100 ml. They also depend upon the speed of fall of the blood sugar. It is sometimes said that a patient has been hypoglycæmic when the blood-sugar level has been relatively high, perhaps 100 to 150 mg. per 100 ml., having fallen rapidly from much higher levels. These cases, if they occur, must be rare. In almost all cases in which the clinical evidence is strong the blood sugar will be found to be well below 100 mg. per 100 ml. After a severe and prolonged hypoglycæmia the blood-sugar level may return to normal although the patient is still unconscious.

The vast majority of cases of hypoglycæmia occur in diabetic patients on insulin treatment. Most diabetics on insulin have had hypoglycæmic attacks on occasions. The frequency with which they occur depends upon the patient's sensitivity to insulin, the care with which the diabetes is controlled and, most important of all, the patient's good sense. The attacks are due to (1) too large a dose of insulin, (2) missing a meal, (3) unusual exertion; or a combination of these factors. Sometimes no cause is found. The attack is likely to be at the time of greatest effect of the insulin or soon afterwards. A patient on twice-daily soluble insulin is most liable to hypoglycæmia in the mornings, especially shortly before the midday meal, and in the early part of the night. Patients taking protamine zinc insulin tend to get reactions during the night and early morning; those on lente insulin may get them at any time, but more often late in the day or during the night. Most patients have warning of an attack, but some, especially those taking long-acting insulins, may not. A patient's insulin requirement is not fixed. It is particularly likely to fall shortly after the original stabilization of the diabetes;

this is a time therefore when hypoglycæmic attacks are common. Sometimes patients may stop insulin altogether because of persistent hypoglycæmia on small doses of insulin but it nearly always has to be resumed later.

Hypoglycæmia can be produced by the sulphonylureas. It is uncommon but cases have been reported, especially among those on chlorpropamide, although the dose has not been excessive.

The amount of insulin needed to produce hypoglycæmia varies greatly from one person to another. Some diabetics, especially older, fatter patients, are resistant to its action and may be able to tolerate an extra 100 units of insulin without effect. But young, thin patients may be so sensitive that an extra 4 units will produce severe hypoglycæmia. This is a much greater sensitivity than is found among most normal people.

SYMPTOMS AND SIGNS

The *symptoms* of hypoglycæmia, too, vary greatly but tend to be the same in any one patient. Mild attacks are usually signalled by feelings of tiredness, emptiness, and lightheadedness. These symptoms are followed by palpitations, tremor, sweating, tingling feelings particularly around the mouth, headache, and visual disturbances. There may be mental confusion, aggressive speech and behaviour, then unconsciousness and convulsions and eventually death. A patient usually recognizes his own pattern of hypoglycæmic symptoms but this does not always mean that he will, or can, treat himself. One of the symptoms may be obstreperous and irresponsible behaviour so that he may violently refuse all attempts to help. The changes of character and behaviour in hypoglycæmia are unfortunately always for the worse: an uncooperative patient never becomes sensible, but the reverse is often true. Whenever a diabetic starts to behave oddly, especially if he is confused or aggressive, the possibility of hypoglycæmia should spring to mind.

The *signs* of hypoglycæmia are produced by glucose lack in the brain and by the body's reaction to the hypoglycæmia. They are pallor, sweating which is often very intense, tachycardia, drowsiness, coma or convulsions. The plantar responses may be extensor in severe hypoglycæmia and in rare cases signs of hemiplegia may appear and persist for some hours.

DIAGNOSIS

The diagnosis depends upon finding a low blood sugar. It is extremely important to take a blood sample in every patient suspected of hypoglycæmia before giving any treatment. If glucose promptly restores the patient to normal and there is no question of any other disease being present, the blood sample can always be thrown away but if there is any doubt it may turn out to be invaluable; indeed, it is likely to be the only way to arrive at a diagnosis in many cases and taking a blood sample during an attack may save endless and fruitless investigations later. If the blood sugar is found to be above about 60 mg. per 100 ml. hypoglycæmia is unlikely

to be the cause of the patient's symptoms provided that (1) no glucose was given before blood was withdrawn, (2) there was no contamination of the blood sample (a minute contamination with 50 per cent. glucose solution wrecks the result). The urine may well contain sugar during hypoglycæmia, even in large amounts, due to the presence in the bladder of urine secreted when the blood sugar level was high.

In most cases the diagnosis is clear from the circumstances of the attack. If there is doubt, giving glucose after taking a blood sample is a good diagnostic test. If this promptly restores the patient to normal, hypoglycæmia is the likely cause of the attack. Giving glucose by mouth or by vein is perfectly safe and never provokes diabetic ketosis or coma. Some textbooks of medicine have contrived to create confusion between hypoglycæmic and diabetic coma. There should be none. Diabetic coma is always of gradual onset after a period of severe diabetic symptoms and is always characterized by great dehydration and overbreathing. In all these particulars diabetic coma is utterly unlike hypoglycæmic coma.

The commonest difficulties in *differential diagnosis* lie in distinguishing hypoglycæmia from (a) functional disorders, (b) epilepsy, (c) cerebrovascular seizures, and (d) cardiac arrhythmias.

TREATMENT

Treatment consists in giving glucose, by mouth if the patient is conscious and cooperative (20 to 50 grammes in water) or by vein if he is not (10 to 25 ml. of 50 per cent. glucose solution is usually enough but sometimes as much as 200 ml. has to be given; there is no point in giving more). The longer the hypoglycæmia has lasted the greater the amount of glucose needed and the slower the response. After prolonged hypoglycæmia a patient may take hours or even days to recover fully. Adrenaline is much less effective than glucose in restoring blood sugar to normal.

After the patient has recovered consciousness it is well to give some carbohydrate-containing food if he is on long-acting insulin as there is a risk of a recurrence of hypoglycæmia.

Although recovery, even from very severe hypoglycæmia, is the rule it can be fatal. Death may follow after several days of coma; at necropsy the brain shows congestion and petechial hæmorrhage in the acute stage; later, loss of cells, especially in the cortex and basal ganglia.

Hypoglycæmia is particularly to be avoided in cases of coronary artery disease and of epilepsy.

D. A. PYKE, M.D., M.R.C.P.
Physician to Outpatients, Department of Diabetes, King's College Hospital.

NOTES AND QUERIES

'Imferon' in Iron-Deficiency Anæmia

QUERY.—I should be glad to know the current view on the employment of 'imferon' in the treatment of iron-deficiency anæmia, which has not responded to oral iron. Is it considered justifiable to use this preparation in an ambulant married women, who denies excessive menstrual loss and claims that she has taken her tablets faithfully? The treatment has been advised by a local anæmia clinic but I am not happy about the matter.

REPLY.—Although the advisability of using intramuscular 'imferon' in the treatment of iron-deficiency anæmia has been questioned recently because of the risk of producing or aggravating neoplastic changes, the evidence is not considered to be very convincing by most experienced hæmatologists who are continuing to use 'imferon' in suitable cases—mainly those who cannot or will not take oral preparations.

In the specific example quoted, if the patient has really taken an *adequate dosage* of iron tablets orally without benefit and without side-reactions, then clearly the next and most important step to take, and one that should have been taken initially before starting any treatment, is to investigate the patient carefully to find the reason for the refractory anæmia and its failure to respond to the oral iron therapy. Search must be made for occult bleeding from the alimentary tract, for steatorrhœa and intestinal disease, for malignant disease of the gastro-intestinal tract, mediastinum or lungs, and for other complications. Only if these prove to be negative should 'imferon' be given in the absence of further clear diagnostic evidence. The whole subject is discussed in detail on p. 224 of this issue.

JOHN F. WILKINSON, M.D., M.SC., PH.D., F.R.C.P., F.R.I.C.

Hypercholesterolæmia

QUERY.—What is the general consensus of opinion on triparanol in the treatment of hypercholesterolæmia?

REPLY.—The general consensus of opinion is that this drug fulfils its manufacturer's claims to reduce the level of blood cholesterol in nearly three-quarters of the people to whom it is given. It does so by arresting the synthesis of cholesterol at the earlier stage of desmosterol. What is not certain is that the patients are any better for having the cholesterol synthesis arrested at this phase, and in my own limited experience the drug has proved least successful in those with the highest blood cholesterol.

H. A. DEWAR, M.D., F.R.C.P.

Alopecia Areata in Childhood

QUERY.—I would be most grateful for your opinion with regard to treatment of a girl, aged 10 years, who is suffering from alopecia totalis (with the exception of a few hairs on her right eyelash) and now has no hair at all on any part of her body. Hair fell from the scalp about three-and-a-half years ago and progressed quickly to complete baldness with, in the past six months, further loss of the few remaining wisps on the back of her head and her eyebrows and eyelashes (except for partial remnants on right eyelash). The skin of her scalp is smooth and shiny with atrophic hair follicles, but some follicles are visible at the periphery. She was pale and underweight (weight 56 lb. [25 kg.]) when first seen in July 1960, with unhealthy cryptic looking tonsils. She had had recurrent tonsillitis, three to four attacks each winter, since the age of 4 years. Since then she has been on iron and vitamins and had her tonsils removed in August 1960, but her general condition has not improved appreciably since and her alopecia has worsened. She is a highly strung child, but otherwise she shows nothing abnormal on clinical examination.

Family history.—Her mother died when the child was 7 months old. Her father works away from home and she has been brought up by, and lives with, a very kind aunt who is her father's sister. There is a family history of alopecia: her father's brother suffered temporary partial alopecia during an attack of rheumatic fever. Her mother's brother also had temporary partial alopecia.

REPLY.—Unhappily there is no effective remedy as yet for alopecia areata, the etiology of which remains unsolved. Psychogenic factors are by no means always discernible, although many of the subjects are 'highly strung' and the alopecia does seem to be triggered sometimes by sudden emotional shock. Most cases recover spontaneously and some do not: treatment makes no real difference. The outlook worsens when there is a hereditary tendency, when relapses are frequent, and if the whole scalp is involved or the alopecia becomes universal.

There may be a place for short-term systemic corticosteroid therapy in the early stages of a rapidly spreading alopecia areata, but steroids are not justified when the alopecia is established. In a proportion of cases treated with cortisone or its analogues a rather unsatisfactory regrowth of hair has occurred but the drugs have no curative effect, the hair only falling out again when the dose is reduced below a certain level. Consequently, indefinite treatment would be required with all the attendant steroid risks

and should not be sanctioned for what is after all a disorder only of cosmetic significance. Interesting results have been obtained by intralesional injection of hydrocortisone or prednisolone, but here again the steroid effect is reversible, the regrowth of hair patchy, and the ultimate prognosis probably not materially affected.

E. W. PROSSER THOMAS, M.D.

Malaria Prophylaxis

QUERY.—My wife and I are going to Lagos later this year for a couple of months. It is clearly wise to take a malaria suppressive when visiting this part of the world and I would value your advice on the most effective drug for this purpose. Other things being equal, it would seem more convenient to use one of the preparations where only a weekly dose is necessary. I shall be most grateful for any help you can give me on this point.

REPLY.—The main points concerning this question are covered by the answer concerning malaria prophylaxis in the June issue (p. 792). The following point, however, is of relevance to the choice of malarial prophylactics taken at weekly or at daily intervals. The incubation period of malaria is approximately ten days. If therefore a prophylactic dose taken at weekly intervals should be omitted, a period, longer than the incubation period of malaria, would be spent unprotected and for this reason there is much to be said for taking a daily dose of prophylactic.

PROFESSOR A. W. WOODRUFF, M.D., PH.D., F.R.C.P., D.T.M. & H.

Perthes' Disease (Pseudocoxalgia)

QUERY (from a reader in India).—What is the latest theory about the pathology of Perthes' disease (pseudocoxalgia) of the hip-joint? What is the present position regarding its management, treatment and prognosis?

REPLY.—The essential pathology of this condition is degeneration of the capital epiphysis of the femur due to avascular necrosis brought about by interference with the blood supply, but the cause is still unknown. Injury is probably an important factor and is supported for the following reasons:—

(1) The condition is commoner in boys and in over half of the cases there is a clear history of injury.

(2) The blood supply to the head of the femur is variable during the age-period when pseudocoxalgia is common and is more likely to be damaged then.

(3) It is known that avascular necrosis of the femoral head occurs after undisplaced fractures of the femoral neck in children during the same age-period.

A constitutional factor may be involved as pseudocoxalgia is sometimes found in families and in twins, and often both hips are involved. The changes also are not always confined to the capital epiphysis but may affect the acetabulum as well. Infection, and endocrine and metabolic disorders have also been blamed, but without convincing evidence.

Management and treatment.—Within recent years views on treatment have changed and the situation is still in a state of flux. All are agreed that treatment during the acute stage, when the hip is irritable, should be rest and traction to reduce spasm and prevent deformation of the epiphysis. Rigid immobilization is unnecessary, however, and traction in bed is sufficient. While revascularization is taking place, weightbearing must be avoided in order to prevent deformation of the soft capital epiphysis. During this phase immobilization, first on a frame and then in a plaster spica, seems unnecessarily drastic, as the results of this treatment are no improvement on those treated as ambulant patients by the provision of a patten-ended weight-relieving caliper. The use of crutches and a sling for the affected leg cannot be recommended as it is difficult to ensure the cooperation of the child and his parents.

Prognosis.—The most important factor is the age. The later the age of onset the more serious the prognosis and at 10 to 12 years the outlook is very bad. Osteoarthritis is inevitable when there is considerable deformation of the head of the femur but symptoms seldom appear until after the age of 25. Probably one-third of all patients develop a normal hip and about one-quarter have a poor result.

F. C. DURBIN, M.B., F.R.C.S.

Thromboangiitis Obliterans

QUERY (from a reader in Ceylon).—A patient of mine has been suffering from a chronic ulcer of the foot due to thromboangiitis obliterans. He has had a lumbar sympathectomy and a skin grafting of the ulcer. The process of healing of the ulcer is still very slow. I shall be grateful for any suggestions that could hasten the healing process as it is now three months since the patient has been to work.

REPLY.—Tobacco smoking appears to have a deleterious effect on patients with thromboangiitis obliterans and should be completely forbidden. Vasodilator drugs and Buerger's exercises probably have no effect in improving the blood supply to the part affected. Perhaps nicotinic acid, 50 mg. three times a day, might be given. If the patient has not had a period of bed rest, this should be given with the foot

slightly below the level of the heart. Obesity, if present, should be corrected with a restricted calorie intake. Supplementary vitamins should be given, particularly vitamin C, which is necessary for wound healing. The patient should be kept warm but heating of the affected limb is harmful. An impaired venous drainage may have rendered the tissues œdematous. A diuretic of the benzothiadiazine group may then be helpful.

Bland local applications only should be used. Local antibiotics are likely to invoke an allergic reaction. Cultures from the ulcer should be taken and sensitivity tests done on any organism which is grown. The appropriate drug to combat the infection must be given systemically although the local concentration may be reduced by reason of the poor blood supply. If the ulcer is very painful, as is often the case in Buerger's disease, crushing of the cutaneous sensory nerve to the part is justified, both to relieve the pain and to increase the local vasodilatation beyond that provided by the lumbar sympathectomy.

P. B. S. FOWLER, D.M., M.R.C.P.

Acetazolamide Following Iridectomy

QUERY (from a reader in South Africa).—I am in charge of a patient who two years ago suffered from glaucoma and within a few months bilateral iridectomy was performed. She made good progress and the intra-ocular pressure is now normal. She insists, however, that the specialist advised her to take 'diamox' (acetazolamide) indefinitely.

Is there any real justification for this expensive drug in view of the fact that she has had iridectomy and the glaucoma is unlikely to recur? Would it be justifiable to stop the acetazolamide and see what happened?

REPLY.—It is extremely difficult to make pontifical statements about a case such as this which one has not seen. It would appear, however, that the patient with glaucoma (type unfortunately not specified) was successfully operated upon and the tension was reduced. There are so many varieties and variations of glaucoma that certainty is impossible, but I would say that it appears that here, operation successfully reduced the tension. In such a case unless there were indications of instability in the tension I certainly would not advise the continued use of acetazolamide, merely because it would seem unnecessary. I would go further, and say that it would be perfectly justifiable to stop using acetazolamide provided the patient were at hand to see whether there is any justification for its continuance.

FRANK W. LAW, M.D., F.R.C.S.

The Meinicke Reaction

QUERY.—A male patient of mine, aged 55, who has never been ill in his life and has been a regular blood donor for 12 years, has been reported as having a slightly positive Meinicke's reaction and a double-positive Laughlen's reaction. What is the significance of these findings? The patient is fit and well, and has no symptoms or physical signs.

REPLY.—It has previously been assumed that a positive result of a Wassermann reaction (that is a complement-fixation test) or of a precipitin reaction (e.g. the Kahn or Meinicke test) indicated syphilis. This belief, however, cannot now be upheld, as evidence has been accumulating that positive results may be obtained in other conditions. There is only one test supposed to be absolutely specific for syphilis and that is the treponema immobilization test. This test is complicated and laborious and could not possibly be performed routinely on a great number of specimens. It is done in special laboratories and, up to now, no cases have come to light in which the specificity of the test would have been doubted.

A positive serological reaction, in the absence of syphilis, has been called a 'biologically false reaction.' Although it is true that in well-treated syphilis or in the initial stages of the disease one or other test may show a positive result, a pattern like the one mentioned is suspect of a 'biologically false reaction'. A great number of conditions may lead to these serological changes. According to the American literature and our own experience, a positive serological reaction follows at least 50% of all primary smallpox vaccinations. It is also common in conditions such as glandular fever, malaria, virus pneumonia and hæmolytic anæmias of the acquired type. Positive serological reactions are also an important manifestation of collagen diseases, in particular of lupus erythematosus, and some authors have claimed that pregnancy by itself may produce one. There is no doubt that there are still other conditions which may produce this picture and the common denominator seems to be a change in the plasma proteins. It is therefore not surprising to find positive reactions in all these conditions as most of them show marked changes in the plasma protein distribution and pattern.

The practical significance of these findings is that the serological changes may be the first signs of an underlying disorder and it would appear important to watch people who exhibit them, both with regard to their general health and to the persistence or otherwise of the abnormal serology. If the serology after small-

pox vaccination is a guide, this may stay positive for anything up to three or four months and for practical purposes, I would suggest that if a repeat specimen gives the same pattern, syphilis should first be excluded by having a treponema immobilization test performed. If this is negative, further observation would be advisable and such investigations as, for instance, sedimentation rate, urine examination and blood studies might help.

W. WEINER, M.D.

Nasal Decongestants

QUERY.—What are the relative merits of nasal decongestants? Would there be any particular application in an aerosol form for spraying around in canteens or factories?

REPLY.—Without any doubt the best vasoconstrictor drug to use in the nose is ephedrine hydrochloride. This is most useful as a solution in normal saline, either 0.5%, 0.75%, or 1%. Many of the more powerful vasoconstrictors result in vasodilatation of the nasal mucous membrane and marked congestion of the mucous membrane in a relatively short time after use. A full discussion of the subject will be found in 'The Practitioner's Handbook' (p. 458).

The use of vasoconstrictor drugs for spraying of canteens, factories, and the like is undesirable.

W. A. MILL, M.S., F.R.C.S.

PRACTICAL NOTES

Relapse in Pulmonary Tuberculosis

'THE importance of prolonged observation of patients with pulmonary tuberculosis after apparent arrest of the disease is emphasized' in a report of the research committee of the British Tuberculosis Association (*Tubercle*, June 1961, **42**, 178). The report is based upon a follow-up of 2,269 patients notified as having pulmonary tuberculosis at 15 centres in England and Scotland in 1947, 1951, and 1954. Of these 2,269 patients chosen at random, 1,862 (82.1%) were traced. In 19.4% of these patients the disease never became quiescent: 45% of those notified in 1947 and 10.8% of those notified in 1954. Among the 171 notified in 1947 who became quiescent, the relapse rate was 3.7% in the first year and 7.9% in the third year, thereafter the relapse rate remained between 1.8% and 4.7% up to nine years. Among the 875 notified in 1954 who became quiescent, the relapse rates for the first four years were: 2.6%, 3.1%, 2.2% and 0.7%, respectively. Attention is drawn to the fact that in the early years of treatment, the patients notified in 1951 had the highest relapse rates of all. This is attributed largely to inadequate chemotherapy, and it is noted that relapses were still recurring in this group up to six or seven years. The significance of this is that 'these survivors of the early period of chemotherapy are the patients most likely to be harbouring resistant strains of *M. tuberculosis*' and 'this constitutes a serious public health menace when relapse occurs and they start to excrete bacilli'. The general conclusion is that 'the likelihood of relapse appeared to be much more influenced by the type and duration of chemotherapy than by the original extent and nature of the pulmonary disease'.

Massive Stilbœstrol Therapy in Carcinoma of the Prostate

TWENTY-FIVE patients with advanced metastatic carcinoma of the prostate were treated with stilbœstrol diphosphate in massive dosage by the intravenous route over a thirty-day period by V. Colapinto and C. Aberhart (*British Journal of Urology*, June 1961, **33**, 171) at the Sunnybrook Hospital, Ontario. For the first ten days the dose was 500 mg. thrice daily; then 500 mg. twice daily for the next ten days; and 500 mg. once daily for the remaining ten days. Thereafter 500 mg. was given weekly as a maintenance dose, to a total dosage of 30,000 mg. over a thirty-day period. The result in fourteen patients was classified as good (complete relief of pain, usually in the first few days; gain in weight, strength and wellbeing; relief of urinary symptoms). In five the result was fair, and a poor result (no relief of pain; progressive downhill course; inability to tolerate the drug) was noted in six cases. Only one patient showed conclusive radiological evidence of regression of metastases and no clinically detectable change in the prostate was observed. It is concluded that 'massive stilbœstrol diphosphate therapy is worth while in advanced carcinoma of the prostate'. Optimum dosage is probably an individual matter but there is some evidence that it should be pushed to the point at which the serum acid phosphatase levels approach normal. For patients who are 'refractory to usual

œstrogen therapy, or who are in relapse after long periods of successful control' this is a useful method of treatment.

Recurrent Vincent's Disease

REVIEWING 61 consecutive cases of Vincent's disease, J. D. Manson and H. Rand (*British Dental Journal*, June 6, 1961, **110**, 386) found that abnormal gingival contours and food impaction were the commonest associated features. Several forms of treatment had been used, including hydrogen peroxide (33 cases), penicillin lozenges or chewing gum (31), chromic acid (25) and systemic penicillin (17). Scaling had been undertaken in 27. 'In few cases treated outside the hospital', it is noted, 'was treatment continued after the acute phase ended', and 'themost important factorin recurrence'appeared to be 'failure to correct gingival deformities caused by the first attack'. Treatment, it is recommended, should fall into two stages: that of the acute phase and that of the residual condition. Because of their necrotizing power caustics such as chromic acid should not be used. Local penicillin with its well-known disadvantages is also best avoided. For the first four or five days attention should be concentrated on removal of debris and necrotic material by frequent use of warm mouthwashes and sponging with cotton-wool soaked in hydrogen peroxide (10 vol.). As soon as possible, usually by the fifth day, a light scaling is undertaken and careful instructions in oral hygiene are given. Factors predisposing to recurrence, such as overhanging fillings or pericoronal flaps, are corrected at this stage. Gingivoplasty may be required. Patients with general malaise, fever and enlarged glands, should be treated in bed with full doses of penicillin or tetracycline. Antibiotic therapy, it is stressed, does not rule out the need for proper local treatment.

Intravenous Urea in Glaucoma

THE preoperative use of urea to reduce ocular tension in three glaucomatous patients resistant to acetazolamide is reported by C. G. Keith (*British Journal of Ophthalmology*, April 1961, **45**, 307). As it is unpalatable, it was administered by intravenous drip. To reduce the tendency to hæmolysis it is used as a 30% solution in 10% invert sugar. The solution 'is freshly prepared and the solvent must be warmed before adding the urea as the dissolution is an endothermic reaction'. As diuresis is rapid and patients may therefore become 'very distressed' if not catheterized before starting to administer the solution, all patients are catheterized, using an indwelling catheter, and placed on continuous drainage. The urea solution is administered over a period of about one hour at the rate of 30 to 40 drops a minute, the total dose being from 1 to 1.5 g./kg. body weight. After about thirty minutes the ocular tension is usually soft enough for the operation to be performed. In the three patients reported on, administration was followed by an immediate reduction in intraocular pressure and none experienced any untoward after-effects. In one case there was troublesome bleeding 'but this may have been due to the congested state of the eye before operation'. The use of urea is not recommended in the presence of renal failure, although no harmful effects have been reported following its use in such cases.

Surgical Hazards in Rheumatoid Arthritis

ATTENTION is drawn by D. L. Gardner and F. Holmes (*British Journal of Anæsthesia*, May 1961, **33**, 258) to the operative and anæsthetic hazards that may arise in patients with rheumatoid arthritis who are submitted to surgical intervention. They give details of five cases to illustrate these hazards: four of these patients died postoperatively. One, a woman aged 33, died of mechanical respiratory difficulty during and after anæsthesia, caused by thoracic immobility and by rheumatoid arthritis of the larynx. Another, a man aged 55, was found at necropsy to have extensive amyloid disease, whilst another, a woman aged 67, died of a fulminating Clostridial infection which was attributed to diminished powers of resistance on the part of the patient. The fifth patient, who survived, had a stormy postoperative period as a result of respiratory difficulty resulting from laryngeal stenosis and ankylosis of the costovertebral joints with almost complete immobility of the thoracic cage. There are thus three major hazards to be guarded against. One is respiratory difficulty resulting from arthritis and ankylosis of the small joints of the larynx, cervical spine, and temporomandibular joints, and costovertebral joints. The second is renal insufficiency from extensive amyloid disease, which has been reported in eight of 50 cases examined post-mortem. The third is an apparent diminished resistance to infection in patients with rheumatoid arthritis.

Mondor's Disease

MONDOR'S disease, or superficial phlebitis of the chest wall, is not so rare as has been suggested, according to C. Honig and R. Rado (*Annals of Surgery*, April 1961, **153**, 589) in reporting seven cases seen in 'a suburban, general surgical practice in a period of eight years'. The disease is a phlebitis and periphlebitis of the lateral thoracic or thoraco-epigastric vein occurring

primarily in women aged 21 to 55, but men are also affected. In the authors' series there were five women and two men. The left side is most commonly affected, and the onset is insidious, progressive and usually painful. Characteristically there is a tender, fibrous cord fixed to the skin and forming a furrow. It is usually situated below the level of the nipple but may be anywhere between the anterior axillary line and the epigastrium. The course is benign and most cases resolve in several weeks to months without treatment. The etiology is unknown, but an etiological factor is suggested in each of the cases reported by the authors: three developed following biopsy for benign lesions of the breast, one followed shaving of the axilla, one was post-partum and the two cases in men were post-traumatic. The importance of the condition is that because of the skin retraction a mistaken diagnosis of cancer of the breast may be made.

Neonatal Heart Sounds

AN investigation has been carried out by M. Braudo and R. D. Rowe (*American Journal of Diseases of Children*, May 1961, **101**, 575) of the findings on cardiac auscultation in the newborn infant. Their investigation was carried out in 82 normal mature infants, in whom auscultation was carried out at half-hourly intervals during the first eight hours of life, and thereafter at random intervals. As a result they present the following 'composite picture of the heart sounds and murmurs in the majority of infants in the new-born period'. Soon after birth the first sound is split and the second sound is single. At a variable time between the second and fourth hours of life, splitting of the second sound becomes appreciable to the ear. In about 15% of infants, usually between the fourth and eighth hours of life, a continuous or crescendo murmur can be heard, and in about 55% an ejection murmur appears at some time during the first day of life. The duration of these murmurs varies from infant to infant. By the age of 16 hours the second sound tends to be well split. On the second day of life, an ejection systolic murmur is still audible in one-third of babies and the second sound is widely split in most. In some infants an early systolic ejection click is heard.

Smoking and Prematurity

THE incidence of prematurity among mothers who smoke cigarettes and those who do not was investigated by T. M. Frazier and his colleagues (*American Journal of Obstetrics and Gynecology*, May 1961, **81**, 988) who carried out a survey in 2,736 negro women. The prematurity rate ranged from 11.1% in non-smokers to 22.9% in those who smoked more than one packet per day. Whilst the over-all rate for smokers was 18.4%, the incidence in the 502 primigravidæ was 'not significant', possibly due to the fact that there were proportionately fewer heavy smokers in this group—only 31% smoked more than half a packet a day compared with 41% of the 2,234 multigravidæ. Although there was a reduced rate of prematurity among the 154 women who stopped smoking during pregnancy, 'there is no evidence that a reduction in prematurity rates could be achieved in a randomly selected group by their curtailing or stopping cigarette smoking during pregnancy. Until the role of smoking and its association with increased prematurity is determined, each obstetrician must decide whether or not to advise his patients to limit smoking'.

Intramuscular Injections

THE anterior gluteal region is the site of selection for intramuscular injections, according to S. Zelman (*American Journal of the Medical Sciences*, May 1961, **241**, 563). The method of localizing the site is shown in the accompanying figure. The tip of the index finger is rested on the anterior superior iliac spine. The third finger is then widely abducted ('to form a V with the index finger as in the Swiss oath or in Sir Winston Churchill's V-for-Victory sign')

and its finger-tip brought to rest just below the crest of the ilium. With the palm of the hand thus resting on the lateral aspect of the thigh, the site of injection is demarcated by the triangle formed by the V of the two fingers and the horizontal ridge of the iliac crest above. The needle is thrust through skin and muscle in a single movement, pointing slightly towards the head, to a depth of 3 to 4 cm. and the injection made after first aspirating to ensure that a blood vessel has not been entered.

REVIEWS OF BOOKS

Thrombosis and Anticoagulant Therapy. Edited by W. WALKER. Edinburgh: E. & S. Livingstone Ltd., 1961. Pp. 106. Illustrated. Price 17*s.* 6*d.*

MOST of us, in our student days, studied Howell's 'Theory of Coagulation' and concluded, usually rightly, that it was too complicated to stay permanently in our minds. Since then the theory has been expanded until now there are at least ten clotting factors and at least as many for the complementary process of fibrinolysis. The international experts who assembled for the symposium of which this volume is the Proceedings comprise world-famous figures to whom words like plasminogen, Hageman factor, and pro-accelerin, are everyday lunch-time table talk. Fortunately for the general reader there is, in this biochemical dough, a leavening of clinical medicine, both its theory and its practice, which lightens it considerably. The general practitioner can learn why so many of his coronary patients and so few of his cerebral ones receive anticoagulants. If he wishes to run his own anticoagulation clinic he can learn how to do it, and what it will cost him. The hospital doctor will find some sound principles upon which to select patients for such treatment, and the super-specialist will receive some excellent information as to why patients to whom he has been providing an artificial circulation for their heart operations tend to bleed excessively then and afterwards.

Like Jack Horner's pie, this book has a hard crust but anyone can put in his thumbs and pull out some plums. If, unlike Master Horner, one has fingers with a reasonable knowledge of modern coagulation theory at their tips it makes very fascinating reading indeed.

Recent Advances in Human Nutrition. By J. F. BROCK, D.M., F.R.C.P. London: J. & A. Churchill Ltd., 1961. Pp. 454. Illustrated. Price 50*s.*

ALTHOUGH a mass of information is packed into this book, it is presented in such an unsatisfactory manner that it is difficult for the reader to find what he is seeking. The major trouble is that the book is really two books. What is described as 'part I' extends to 175 pages and is written by Professor Brock himself. Part II, entitled 'invited contributions on special subjects', consists of fifteen chapters, each by different authors, dealing with a variety of nutritional problems.

Part I is, on the whole, a balanced survey of the subject, though cross-references to part II make it difficult reading. Part II is such a heterogeneous collection of articles that it is difficult to understand how they have ever found their way into a book such as this. One of them, entitled 'Nutrition in old age', has the running headline 'German literature' and there is an editorial note to the effect that there has been 'a misunderstanding' over the subject dealt with. This is certainly not the high standard that we have come to expect from this publisher and this series. On the other hand, the seeker after knowledge will find many useful facts tucked away within its pages.

Management of Hypertensive Diseases. By JOSEPH C. EDWARDS, A.B., M.D., F.A.C.P., F.A.C.C. London: Henry Kimpton; St. Louis: C.V. Mosby Co., 1960. Pp. 439. Illustrated. Price £5 12*s.* 6*d.*

THIS is a scholarly and up-to-date account of the management of hypertensive disease by an American physician who has obviously great practical and theoretical knowledge of the subject. There is a good account of the present concepts of the nature of hypertensive disease, of the effects of hypertension on the heart, and of the special problems of hypertension in pregnancy. Views of the current, rapidly changing, use of anti-hypertensive drugs are described in detail, with inclusion of all drugs which are generally used and out of the purely experimental stage of their development. There is a complete coverage of the vast modern literature on this subject, 1,622 separate references being quoted. British and Commonwealth literature as well as that from the United States is fairly quoted, although European authorities will probably feel that their work has been somewhat neglected. Hypertensive disease best treated by surgery, e.g. that secondary to adrenal or unilateral renal disease and that secondary to coarctation of the aorta, is especially well described.

This is a valuable book of reference for the established worker on the management of hypertensive disease, but cannot be recommended for the student or the junior post-graduate worker, as it is too much a detailed review of recent work to be regarded as a suitable introductory text. The 68 figures are clear, informative and well reproduced. Whether the inclusion of 45 representative case histories is of value will be a matter of personal opinion. Most readers will feel that they needlessly break the continuity of the text and make the book more of a long review with inclusion of personal experience, than a typical monograph of a difficult and rapidly changing branch of current medical practice.

Clinicopathological Conferences of the Massachusetts General Hospital. Edited by BENJAMIN CASTLEMAN, M.D., and H. ROBERT DUDLEY, JR., M.D. London: J. & A. Churchill Ltd., 1960. Pp. 295. Illustrated. Price 90*s*.

IN their preface, the editors attribute to Langdell the first introduction of the 'case system' of teaching, and credit Cabot with its first application in systematic medical teaching in 1900. The clinicopathological conferences of the Massachusetts General Hospital are now almost as widely known in Western Europe as they are in America, and the popularity of this system of teaching is evidenced by the fact that certain British medical publications now incorporate 'case conferences'. To those unfamiliar with these it should be explained that the 'conference' is essentially an exercise in the analysis of the case history and clinical findings and their correlation with the results of diagnostic investigations. In other words, it constitutes a reasoned clinicopathological approach rather than an exercise in 'pin-point' diagnosis. This volume presents a series of fifty cases (all of which have previously been reported in the *New England Journal of Medicine*). Those familiar with the high standard of these conferences will find much interesting reading in this book, and it will also provide a useful exercise for those at present engaged in their specialist studies. The publishers and editors are to be congratulated on their selection of material, the excellent way in which it is presented, and the fine quality of the illustrations.

Lipids and the Steroid Hormones in Clinical Medicine. Edited by F. W. SUNDERMAN, M.D., PH.D., SC.D., and F. W. SUNDERMAN, JR., M.D. Philadelphia: J. B. Lippincott Co., 1960. London: Pitman Medical Publishing Co. Ltd., 1961. Pp. 207. Illustrated. Price 85*s*.

THIS book reports the proceedings of a conference held in Washington under the auspices of the Association of Clinical Chemists. It deals mainly with methods for the quantitative determination of the various lipoids and steroid hormones in body fluids but also includes chapters in which the clinical significance of such estimations is discussed. Many of those contributing are recognized authorities in their own fields and for this reason the general standard of presentation is high. In the first section details are given of modern methods for estimating the serum concentration of total lipoids, cholesterol and its esters, phospholipoids, total fatty acids, free fatty acids and lipoproteins. There are also valuable contributions on the clinical significance of raised blood lipoid levels and on the prognostic value of cholesterol and phospholipoid determinations in patients with arteriosclerotic heart disease. The second section discusses recent trends in methods for estimating corticosteroids, 17-oxosteroids, œstrogens and progesterone and its metabolites. Special attention is given to radioactive techniques and to procedures involving partition chromatography. The chapter on the clinical significance of assays of corticosteroids and 17-oxosteroids presents a clear and authoritative account of a highly complex subject and is somewhat more modern in its content than the corresponding chapter dealing with œstrogens and progesterone metabolites.

This book presents a large volume of highly specialized information in a very readable form. It should prove of value to biochemically minded endocrinologists, to general physicians and to workers in hospital laboratories.

Complications in Surgery and their Management. Edited by CURTIS ARTZ, M.D., F.A.C.S., and JAMES HARDY, M.D., F.A.C.S. Philadelphia and London: W. B. Saunders Co., 1960. Pp. 1075. Illustrated. Price £8 10*s*.

THIS monumental encyclopædia on the complications of surgery and the surgery of complications has a clear place in any surgical library. It deals with the complications in every system that may follow operations (and even non-operative procedures employed in surgery) on every organ or structure in the body. The publishers have taken every trouble to make the work as complete and as authoritative as possible. They have brought together a group of writers whose names as surgeons are known throughout the world, and they have given them every assistance in the way of illustrations. The editors start with the apt quotation from Alfred Worcester: 'Harbours are made safe for mariners not by records of prosperous voyage, but by buoying the dangerous reefs and sunken ledges that have caused disasters'. True enough. But a mariner who carries charts showing every rock, reef, and sunken ledge in every harbour in every bay, inlet or channel in all the seas of the world would spend all the time in the chartroom. A wise mariner, entering an unknown harbour for the first time, employs a pilot.

The difficulty about this careful book is its very completeness. Unless a surgeon has spent some hours reading up the possible complications of an operation he intends to perform the next day, should unexpected difficulties arise he will be confused rather than helped by the wealth of the alternatives offered to him. Take

the common complication of venous thrombosis and pulmonary embolism, for instance; so many alternatives are offered in chapter 15, many of them highly theoretical, most of them requiring the experience of maturity to evaluate them, that the anxious operator would probably be well advised to shut up the book and seek the personal guidance of a wise senior colleague.

Radiation Injury in Man. By EUGENE P. CRONKITE, M.D., and VICTOR BOND, M.D., PH.D. Springfield, Illinois: Charles C Thomas; Oxford: Blackwell Scientific Publications, 1960. Pp. 200. Illustrated. Price 52*s*.

RADIOBIOLOGY is as broadly based as biology itself, so that it is impossible even for the radiobiologist to be comprehensively knowledgeable. Two research physicians have undertaken the task of presenting radiobiology to the ordinary doctor of medicine, who in this 'atomic age' may not only have to deal clinically with cases of radiation-injury but as always 'to give an authoritative answer to the questions of individuals who may be rightly concerned about the potential effects of radiation'. They have succeeded in giving a clear account of readable length in plain American language without jargon or complex mathematical physics of the basic principles, current trends of research and clinico-pathological aspects of radiation injury. There is a useful glossary of the technical terms and units, an index and about 100 references. It is a pity therefore that the publishers charge so much considering that their own job of proof reading has been sloppily done.

An Approach to Occupational Therapy. By MARY S. JONES, M.C.S.P., M.A.O.T. London: Butterworth & Co. (Publishers) Ltd., 1960. Pp. 245. Illustrated. Price 42*s*.

THIS book is a survey of 4,115 patients treated at a residential centre for occupational therapy. The author first takes us round and tells us a little of the history of the centre, its site, its staff, the sort of cases that are referred and where they come from. We are told of the admitting procedure and the short introductory talk before going into the workshops. Thus having set the scene the door is opened, so to speak, and the general layout of the workshops is explained, the equipment described, the type of work most helpful for specific disabilities discussed, gadgets, splints and the modifications of workshop equipment necessary to afford maximum benefit in specific cases are considered. The whole is fired by the author's enthusiasm for reablement and, although this is a practical book, its approach is lighthearted, optimistic and at times even humorous. Its modest title is misleading; this is real occupational therapy and this excellent book can be unreservedly recommended to all interested in helping the disabled.

Your Bread and Your Life. By DORIS GRANT. London: Faber & Faber Ltd., 1961. Pp. 244. Price 13*s*. 6*d*.

ALTHOUGH the dominating feature of Mrs. Grant's book is the condemnation of white bread, the opportunity is taken to indict the chemical additives to nearly every foodstuff in the average dietary. Whole-wheat with all its advantages is recommended with the invocation to housewives to be their own baker and indeed their own miller. One fears that the average reader may be terrified to eat or drink anything at all when confronted with such statements as that bleached flour though slower in toxicity is just as certain as cyanide, and the list of food adulterants which may be responsible for almost every disease and disability from juvenile delinquency and varicose veins to mental disturbances, diseases of degeneration and cancer.

As a simple realist, one wonders if many will be persuaded to substitute a 'mulsh', which is a mixture of wheat germ, raw oats, raisins, nuts, grated apples, lemon juice, honey and top milk for the conventional breakfast of eggs and bacon, toast, marmalade and (the disparaged) refined white sugar. Nor will it be easy to convince a child that he should abandon sweets, and chew a raw carrot. To venture on the danger of creating food-faddists is not to depreciate a well-written, well-documented compilation of value to all interested in dietetics but the reader without some scientific education will feel inclined to wonder that we are alive at all.

Principles of Medicine: An Integrated Textbook for Nurses. By JAMES VERNEY CABLE, M.D., M.R.C.P., F.R.A.C.P. Christchurch, New Zealand: N. M. Peryer Ltd., 1960. Pp. 661. Illustrated. Price 55*s*.

THIS book is a refreshing change from the standard type of textbook for nurses; basic anatomy, physiology and elementary pathology are well integrated with the principles of medicine in a concise yet clear and logical approach. The opening chapters, dealing with the nature of disease and the scientific attack on infection, provide a stimulating and interesting presentation, but such terms as 'infiltrate', 'metastasize' and 'achlorhydria' should be explained when first used in the text. It is pleasing to read such a clear explanation of the mechanism of allergic reactions and of blood groups and transfusion precautions, and an excellent yet simple account of body fluids. The author is also to be

congratulated on his concise and up-to-date descriptions of current therapy and simple laboratory investigations. Such a well-produced book, amply illustrated with diagrams, x-ray and photographic reproductions should prove popular with student nurses in the United Kingdom as well as those in New Zealand.

NEW EDITIONS

Progress in Clinical Medicine, edited by Raymond Daley, M.D., F.R.C.P., and Henry Miller, M.D., F.R.C.P., D.T.M., in its fourth edition (J. & A. Churchill Ltd., 50s.) continues to subserve its original useful function of describing the main developments in general medicine, with an essentially clinical orientation. Inevitably when additions to a new edition include subjects such as space medicine and auto-immunity, it is difficult to maintain a clinical 'orientation', but the editors and their team of relatively young authors are striving manfully to preserve this outlook. This can still be recommended to the practitioner as a useful and readable guide to the modern practice of medicine.

A Synopsis of Children's Diseases, by J. Rendle-Short, M.D., M.R.C.P., D.C.H., third edition (John Wright & Sons Ltd., 42s.).—The third edition of this book by the new Professor of Child Health in the University of Queensland will be welcomed by students, by family doctors, by candidates for child-health diplomas and by their teachers. In the course of a good revision some minor errors of previous editions have been removed, and some new syndromes have been briefly described; certain paragraphs on conditions that are becoming less common have been abridged, and others associated with recent advances have been enlarged. References, usually to review articles, are now given for certain diseases but it is not clear why this was done for some and not for others. The book is well produced and well printed and is now a useful member of the 'Synopsis' series.

Modern Occupational Medicine, edited by A. J. Fleming, M.Sc., M.D., F.A.C.P., and C. A. D'Alonzo, M.D., F.A.C.P., second edition (Henry Kimpton, 90s.).—Skilful editing combined with the fact that all twenty-three contributors to this excellent textbook are on the staff of the same chemical company, has made this a more coherent work than is usual with multi-author volumes. In this second edition the previous material has been extensively revised, and two valuable chapters on chest diseases and psychiatry added. The cover is wide, and includes among the expected subjects some less often discussed such as immunization in industry, and the rehabilitation of the alcoholic. The American origin is not obtrusive, and whilst the slant is naturally towards the chemical industry other aspects are not forgotten. Two commendable features are the development of the various themes from first principles: e.g. the physiology of muscular work, and the posing of questions which managements should ask themselves. Indeed much of the book could be read by personnel directors and factory managers with great profit, and the reviewer will certainly circulate his copy.

One found little to query adversely, except the statements (p. 483) that 'aluminium also is a marvellously effective prophylactic against silicosis' and that there is some doubt that aluminium can act as a pathogen. All-in-all, however, this book can confidently be recommended as one of the most useful and stimulating books for the industrial medical officer.

A Handbook of Tropical Diseases, by J. C. Banerjea, M.B., M.R.C.P., and P. B. Bhattacharya, M.B., D.T.M., in its sixth edition (Academic Publications, 45s.) is a book designed for practitioners in India and only diseases prevalent there are included in it; there are therefore no descriptions of yellow fever, schistosomiasis or onchocerciasis. The emphasis throughout is on clinical aspects of treatment in which it fairly reflects current Indian views and practice. There are new chapters on giardiasis and tropical eosinophilia and appendixes on the diagnosis of fevers and of diarrhœas in the tropics; there is also a therapeutic guide. All these are admirable and the practitioner and student in India will find them useful. On the debit side modern therapeutic practice is not always given emphasis; thus 6½ pages are devoted to the use of quinine preparations in malaria and only half-a-page to chloroquine; more space is given to the use of chaulmoogra and hydnocarpus oil in the treatment of leprosy than to sulphones. The emphasis on many points is out of line with current thought and data, thus there is no reference to the value of proguanil as a suppressive and the advisability of avoiding it for schizonticidal use in malaria.

Readers must be selective in using this book but there is much useful information in it.

The contents of the September issue, which will contain a symposium on 'The Infective Diseases,' will be found on page A 118 at the end of the advertisement section.

Notes and Preparations see page 257.
Notes from the Continent see page 261.
Fifty Years Ago see page 263.
World Health News see page A 11.
Motoring Notes see page A 89.
Travel Notes see page A 93.
Bridge Notes see page A 97.
From a Sussex Window see page A 99.

NOTES AND PREPARATIONS

NEW PREPARATIONS

'SOLUVONE' single-dose vials each contain 500,000 units of penicillin (sodium salt) and streptomycin sulphate equivalent to 0.5 g. base, and are indicated in the treatment of mixed infections due to gram-positive and gram-negative pathogens. Advantages are said to include the rapid attainment of peak levels and the possibility of dual action of the two drugs delaying development of resistant strains. Available in boxes of 5, and also as five-dose vials in boxes of 10. (Distillers Co. (Biochemicals) Ltd., Broadway House, The Broadway, Wimbledon, London, S.W.19.)

'SYNOMETRINE' ampoules each contain 0.5 mg. of ergometrine maleate B.P. and 5 units of synthetic oxytocin and are intended for use in the prevention and control of post-partum blood loss in hospital and domiciliary practice. They are said to combine the advantages of rapid onset of oxytocic action, 'which is maintained by the ergometrine', and simplicity of administration. Available as ampoules of 1 ml. in boxes of 6 and 100. (Sandoz Products Ltd., Sandoz House, 23 Great Castle Street, London, W.1.)

PHARMACEUTICAL NOTES

DISTILLERS CO. (BIOCHEMICALS) LTD. announce that 'distampin injectors', which are included in the Ministry of Health list of disposable injection units for which payment is allowable, are now generally available. These injectors are sterile, hermetically sealed units ready for immediate use, consisting of an ampoule holding, under gas pressure (sterile air), one dose of the solution for injection, attached to a sterile hypodermic needle by a transparent plastic tube. When the cover has been removed and the needle inserted into the tissues, the injector is activated by breaking the shank of the ampoule (as in breaking a matchstick), the gas pressure inside the ampoule automatically ejecting the solution into the tissue. The entire injector is then discarded. The unit also contains a filter which prevents any glass particles escaping from the broken shank. In addition, aspiration can be conducted by squeezing and releasing the flexible polythene tube. The preparations available in this form are Injection of procaine penicillin B.P. ('distaquaine' suspension) and Injection of streptomycin sulphate B.P. ('streptaquaine' 1 in 4). (Broadway House, The Broadway, Wimbledon, London, S.W.19.)

IMPERIAL CHEMICAL INDUSTRIES LTD. announce the introduction of 'disulphine blue' for intravenous injection, each ampoule of which contains a 6.2% w/v sterile solution of sulphan blue. The preparation is intended for use as 'a simple and direct visual test of the state of the circulation in normal and damaged tissues'. It is said to be of particular value in the accurate diagnosis and surgical management of burns and soft-tissue trauma, especially the more severe crush and torsion avulsion injuries. Available as ampoules of 10 ml. in boxes of 10. (Pharmaceuticals Division, Fulshaw Hall, Wilmslow, Cheshire.)

FILM NEWS

Diuresis (35 mm. or 16 mm., colour, sound; running time 48 minutes; available in five languages) describes with remarkable clarity the modern conception of renal function generally together with the pathogenesis and treatment of œdematous states. Produced by Dr. G. Munck of Stuttgart it has an international approach and those taking part include distinguished physicians from both sides of the Atlantic. Available on free loan from CIBA International Film Service, Horsham, Sussex.

Perineal Repair (16 mm., colour, sound; running time 20 minutes) is designed to teach a technique of perineal repair to be carried out either in the home or in hospital. It is intended for showing to audiences of general practitioner obstetricians, medical students attending courses in obstetrics, and 'would be of interest to pupil midwives'. Made at the Simpson Memorial Maternity Pavilion of the Royal Infirmary, Edinburgh, and produced by Eothen Films Ltd., the film is available on free loan to groups of doctors and to members of the allied professions, upon application to Duncan Flockhart & Co. Ltd., at their London Office, 4 Carlos Place, London, W.1, or to their representatives.

Competition for Medical Films.—In order to encourage the production of medical films, the Council of the British Medical Association are prepared to award medals and certificates for 16-mm. medical films to be submitted in open competition. Awards will be considered in two categories—one for commercial and one for non-commercial film producers. The choice of subject is left to the competitor. Entry forms and further details may be obtained from the Secretary, British Medical Association, B.M.A. House, Tavistock Square, London, W.C.1.

Food Hints for the Over 60's (25 frames) and *Children's Feet* (30 frames) are two new 35-mm. filmstrips in the useful 'Camera Talks' series. Both are available, price £2 12s. 6d. each including notes, from Camera Talks, 23 Denmark Place, London, W.C.2.

B.M.A. PRIZES AND SCHOLARSHIPS

C. H. Milburn Prize, 1961 (£100) for an essay or study on the subject of medical jurisprudence and/or forensic medicine. Open to any medical practitioner registered in the British Commonwealth, the Republic of Ireland or the Republic of South Africa. Closing date: October 31, 1961.

Sir Charles Hastings and Charles Oliver Hawthorne Clinical Prizes, 1962 (£75 and £50) for the two best entries based upon systematic observation, research and record in general practice. Open to any member of the Association engaged in general practice. Closing date: November 30, 1961.

Prizes for Provisionally Registered Practitioners, 1962 (£50 each) for essays on 'What Contribution Can the Doctor Make Towards the Prevention of Accidents?'. Open to any medical practitioner who registered provisionally on or after June 30, 1960. Closing date: December 31, 1961.

Nathaniel Bishop Harman Prize, 1962 (£100) for research in hospital practice, to be awarded for the best report on original clinical research in a form suitable for publication. Open to any registered medical practitioner on the staff of a hospital in Great Britain or Northern Ireland who is not a member of the staff of a recognized undergraduate or postgraduate medical school. Closing date: January 31, 1962.

Prizes for Medical Students, 1962 (£25 each) for essays on either 'The Doctor-Patient Relationship In and Out of Hospital' or 'The Desirability of a Knowledge of the Arts Subjects in the Practice of Medicine'. Open to any medical student who is a registered member of a medical school in the British Commonwealth, the Republic of Ireland, or the Republic of South Africa at the time of submission of the essay. Closing date: December 31, 1961.

Brackenbury Prize, 1963 (£100) for the best contribution on 'British Medicine: Its Influence Overseas in the Past and Problems for the Future'. Open to any member of the Association. Closing date: December 31, 1962.

Ernest Hart Memorial Scholarship (£300), *Walter Dixon Memorial Scholarship* (£300) and four other research scholarships (£200 each), all tenable for one year from October 1, 1962, for candidates whom the science committee of the Association recommend as qualified to undertake research in any subject relating to the causation, prevention, or treatment of disease. Preference will be given to applications from members of the medical profession. Closing date for applications: February 1, 1962.

Full details regarding all these awards may be obtained from the Secretary, British Medical Association, B.M.A. House, Tavistock Square, London, W.C.1.

DOMICILIARY MIDWIFERY

In conjunction with the College of General Practitioners, there is to be a symposium at the Royal College of Obstetricians and Gynæcologists on Wednesday, October 18, 1961. The meeting is primarily for those in general practice who hold the Diploma in Obstetrics of the R.C.O.G., but will be open to any Member or Fellow of the College who wishes to attend, and if room permits it is hoped to throw open the meeting to any medical practitioner. The morning session will be devoted to ' "The Avoidable Factor" in Maternal Mortality', and the speakers will include Sir John Peel, Professor T. N. A. Jeffcoate, Mr. Arnold Walker and Mr. Frank Stabler. The afternoon session will be devoted to 'The staffing and management of a General Practitioner-Obstetrician Unit and the part it should play in the Obstetric Services'. The opening speakers will include two consultants, Mr. John Stallworthy and Mr. R. A. Tennent, and two general practitioners, Dr. T. Maurice and Dr. P. B. Bailey.

Those wishing to attend should apply before October 4, to the Secretary, Royal College of Obstetricians and Gynæcologists, 27 Sussex Place, Regents Park, London, N.W.1.

RECORD CARDS

The College of General Practitioners now have available the following record cards, designed to fit into the N.H.S. envelope, which they are prepared to issue to non-members as well as members. An *Obstetric Record Card* (12*s*. 6*d*. a 100), a *Summary Card* (12*s*. 6*d*. a 100), and a *Menstruation Chart* (16*s*. a 100). Also available are *Language Cards* (5*s*. a set), printed in French, Spanish, Italian, German, Hungarian and Polish, to assist in history-taking when the patient has little or no knowledge of English. Obtainable upon application to the Secretary of the College, 41 Cadogan Gardens, London, S.W.3.

SOCIAL SECURITY RECIPROCITY

The reciprocal social security agreement which the United Kingdom concluded with the Federal Republic of Germany on April 20, 1960, has now been ratified and comes into force on August 1, 1961.

CANCER RESEARCH

The thirty-eighth Annual Report, for 1960, of the British Empire Cancer Campaign declares that, with more than a million pounds a year to spend, we are 'in the midst of a revolution in cancer immunology, virology and nucleic acid biochemistry, which is almost daily throw-

ing up a wealth of ingenious ideas'. This massive document, more than 700 pages in length, testifies to the wide scope both of fundamental research and therapeutic endeavour that, with gathering momentum, is bringing increasing results. Typical of the work being supported by the Campaign is the study by Churchill-Davidson and his colleagues in the Radiotherapy Department of St. Thomas's Hospital of the effect upon tumours of irradiation under high oxygen tension. Since 1955 they have treated 108 patients selected on the basis that they were thought to have 'little, if any, chance of cure by conventional radiotherapy'. Initial results are described as 'encouraging', and in 15 to 20% a 'really dramatic' response to treatment has been observed.

THE MEDICAL DIRECTORY 1962

THE Editor of *The Medical Directory* writes:—'The posting of the annual schedule for The Medical Directory 1962, to all traceable members of the profession, has recently been completed. Any doctor who has not received the annual schedule, or who has mislaid it and would like to have a duplicate, is requested to communicate as soon as possible with The Editor, The Medical Directory, 104 Gloucester Place, London, W.1. The full name and year of qualification of the doctor should be sent for identification'.

STUDENT HEALTH IN BELFAST

ALTHOUGH the general health of students at Queen's University, Belfast, is noted as 'excellent' in the Student Health Committee medical officer's annual report for the academic year 1959-60, the number of cases of psychoneurosis 'showed quite an increase over previous years and included a larger number of more severe types' requiring specialist consultation or prolonged hospital treatment. Whilst it was considered that many would have broken down in any walk of life, in a few cases this was probably due to the 'special strain and stress peculiar to university life, where competition is now so great a factor and success or failure are decided entirely by examinations'. To the ever-increasing number of students on grants failure usually means the end of their university career and 'with this nemesis hanging over them' many give up all outside interests in favour of work, with disastrous results. It is the detection of the early signs of anxiety and persuading the student that he or she requires help that 'must constitute one of the more important aspects of any student health service'.

CHESS FOR THE BLIND

'INTERNATIONAL chess for the blind has come to stay', according to H. H. Cohen, writing in the May number of *The New Beacon* (1961, **45**, 134). 'The First Chess Olympia for the Blind' was held at Meschade from March 26 to April 2 and was felt to be outstandingly successful. Seven European countries took part, and the standard of play reflected the care with which teams had been chosen and prepared. Yugoslavia won with 22 game points; Great Britain tied with West Germany II in 5th place with 13½ points. This meeting was so successful that the International Braille Chess Association is to press for the expansion of existing national organizations for chess for the blind and the creation of new facilities.

LONGEVITY IN THE U.S.S.R.

IN Britain 0.3 per 100,000 of the population may confidently expect to top their century. In the Soviet Union, however, the chances of becoming a centenarian are at least thirty times as great according to a recent report, whilst in some parts of the Union, such as Azerbaijan, with its 84 centenarians per 100,000, the chances improve more than 250 per cent. The census upon which this is based shows that there are 21,708 centenarians in the U.S.S.R., 592 of whom are 'at least over 120.'

AN EDIBLE DENTAL PROP

COMMENTING on the difficulties many anæsthetists experience with children, Massey Dawkins (*Brit. dent. J.*, 1961, **110**, 315) suggests the use of a dental prop made of suitably flavoured and coloured lozenge paste. Poured into a mould this substance sets hard enough to serve its purpose efficiently. A tape passing through a hole prevents premature swallowing or accidental inhalation. It is claimed that this ingenious idea eliminates some of the initial fear and consequent lack of cooperation on the part of young children. Furthermore it can be used to reward, and console, the patient in the recovery room.

CIGARETTE SMOKING

'PROPAGANDA against cigarette smoking seems to make no progress against the concentrated trade advertisements and until the smoking of cigarettes is as socially unacceptable as the chewing of tobacco, youth will continue to accept the risk'.—Dr. A. Anderson, medical officer of health for Heston and Isleworth, in his annual report.

BANANAS AND GASTRIC SECRETION

BANANAS have a high content of 5-hydroxytryptamine (5-HT) which has an inhibitory action on acid gastric secretion. R. K. Sanyal and his colleagues (*J. Pharm. Pharmacol.*, 1961, **13**, 318) therefore investigated the effect of bananas on gastric secretion in guinea-pigs.

They found that the feeding of bananas reduced the average acidity following the injection of histamine from 15.3 to 2.4 ml. Further, guinea-pigs, in which chronic hyperchlorhydria had been induced, developed a fatal perforation of the stomach by the fifth day when fed their usual diet, but when fed bananas there was no evidence of ulceration of the stomach when the animals were killed.

In other words, 'banana emulsions introduced directly into the stomach reduce acid gastric secretion, and also prevent chronic ulceration and perforation induced by repeated injections of histamine'. Whether these findings have any clinical application is now being investigated.

BODY FATNESS IN WOMEN

ACCORDING to an investigation carried out by C. M. Young (*N.Y. St. J. Med.*, 1961, **61**, 1928), in 94 middle-class young women, aged 18 to 28, the percentage of body weight as fat in young women ranges from 15.81 to 38.62, with a mean of 28.69 ± 4.856. On average, the young women had over two-and-a-half times the percentage of their body as fat as do young men of comparable age and status. The figures for young women were slightly higher than those for middle-aged men and similar to those of elderly men. The conclusion is reached that, in the absence of facilities to make density measurements, the simple technique of skinfold thickness in the abdominal midline, midway between the umbilicus and symphysis pubis, measured with a calibrated caliper gives a better indication of relative fatness than the more elaborate chemical procedures at present in use.

PUBLICATIONS

Drugs in the Treatment of Disease is a collection of 65 articles published in the *British Medical Journal* between 1958 and 1960. For the production of this book they have been revised by their respective authors. Between them they present a useful practical survey of drug therapy at the present day. The standard is commendably high, though it is disturbing to find that so much importance is attached to the experimental carcinogenic effect of parenteral iron, and the strictures on the potentialities of some of the newer amœbicides scarcely seem justified. (British Medical Association, price 35*s.*)

Surgery is Destined to the Practice of Medicine, by Sir Reginald Watson-Jones, B.SC., M.CH. ORTH., F.R.C.S., F.R.A.C.S., F.R.C.S.E., F.A.C.S.— This reproduction of the Hunterian Oration of 1959, is the declaration of faith of a great orthopædic surgeon. It is well produced and beautifully illustrated, and is a bibliophil's treasure. (E. & S. Livingstone Ltd., price 21*s.*)

The Future of Occupational Health Services, a report of the Council of the British Medical Association, calls for the establishment as soon as possible of a comprehensive Occupational Health Service which should be the responsibility of a Government Department. The primary function of such a Service would be 'to take into industry and other employment the full range of medical knowledge, with a view to preventing accident and illness and improving the health of all at work'. Recommendations are made about the relationship between doctor and management and the special needs of adequate undergraduate and postgraduate instruction are emphasized. (British Medical Association.)

Occasion for Ombudsman, by T. E. Utley, examines the Danish office of Ombudsman, or grievance man as he is sometimes called, and the author, who is a well-known political commentator, considers whether such an appointment would be a real contribution to our needs in this country. The arguments, both for and against, and their relevance to many potential sources of conflict, including the operation of the National Health Service, make this book of outstanding interest to all who value human freedom in a Welfare State. (Christopher Johnson, price 15*s.*)

Biblical Leprosy. A Suggested Interpretation, by R. G. Cochrane, M.D., F.R.C.P., is a fascinating exposition of the reasons why 'Biblical leprosy' is not 'leprosy' as we recognize it today. Written by the leading leprologist of the present day it makes out a most convincing case. (Christian Medical Fellowship, price 1*s.*)

OFFICIAL PUBLICATION

Domestic Food Consumption and Expenditure: 1959, the annual report of the National Food Survey Committee, reveals that 'convenience' foods (labour-saving, prepared, or semi-prepared products) accounted for nearly one-fifth of total household food expenditure in 1959. Examination of the effect of the housewife's age upon the household diet showed that food expenditure rose 'fairly sharply' between the ages of 20 and 40 'but thereafter declined with increasing age'. Between 1957 and 1959 the average expenditure on food among old age pensioners rose by 10% compared with an average rise of 4% for all other households, but this was partly accounted for by the increase in pension rates in January 1958. (H.M. Stationery Office, price 8*s.* 6*d.*)

NOTES FROM THE CONTINENT

A European Newsletter

FRANCE

Mortality in Western Europe.—In noting the 'considerable reduction in mortality' in Western Europe in the first half of this century, with the increase in the average expectation of life of almost twenty years, J. C. Chasteland forecasts equally important advances in the next fifty years. He stresses that it has been shown repeatedly that the average life-span is more closely related to the 'medico-social' arrangements in a country than to the standard of living judged in purely economic terms, the Scandinavian countries being a particularly good case in point. Death rates for males, however, have risen during the period under review, and this has been mainly noticeable in the 40 to 60 age-group, and particularly in France and Finland.

In the latter all ages except the first year of life are involved; whilst in France it seems that the years of middle age bear the main brunt. Male death rates show the least rise of all in the Scandinavian countries and the Low Countries. This is probably not solely due to improved standards of living because these countries, which have experienced a marked rise in economic prosperity, show a greater increase in over-all mortality than certain poorer countries, for example Spain and Italy. In France, at any rate, this may be associated with the problem of alcoholism, a problem that is at long last receiving its due meed of attention.

'Blue attacks' and prematurity.—A possible improvement in the treatment of the attacks of apnœa accompanied by cyanosis (the so-called 'blue attacks'), which are so liable to occur in premature infants, is discussed by F. Alison and M. Courtois, who draw attention to the fact that post-mortem studies do not always reveal cerebral or pulmonary lesions sufficient to explain death. They regard a fatal outcome, in some instances at least, as primarily the result of biochemical disturbances. The treatment they recommend is the intravenous infusion of the following solution: Plasma 25-50 ml., Ringer's solution 35 ml., 50% glucose 15 ml., oxytetracycline 20 mg., and 'spirogene' (ammonium phthalamate) 1 ml., to be given at the rate of 75 to 100 ml. per kilogram of body weight per day. Of 14 infants treated with this solution 10 survived. This is felt to have been an encouraging result in view of the accepted mortality of about 50%, and, it is claimed, justifies further inquiry.

Etiological factors in lung cancer.—The difficulties in separating the effects of various etiological factors in bronchial carcinoma are stressed by J. Fauvet, who considers that the elimination of industrial fumes and smoke is one of the chief preventive measures open to the community. Any significant reduction in tobacco consumption is hardly practicable, 'especially when many doctors, themselves convinced of its harmfulness, continue to smoke so heavily'. Filter tips, he considers, are useless in prevention, and, although the choice of cigarette paper and the chemical processes to which it is subjected are doubtless of importance, it is hardly possible to eliminate the 'precursors' of the carcinogens themselves by any means known at present.

The major problem, as he sees it, is atmospheric pollution. He therefore recommends that residential areas be situated away from industrial centres and that every possible step be taken, by legislation if need be, to suppress factory smoke, exhaust gases (especially diesel fumes), and smoke from domestic hearths. These are all practicable and, in Fauvet's opinion, by these measures the rise in the incidence of lung cancer could be halted, and in time a reduction in the number of new cases would follow.

Mitral angina.—P. Chiche and his colleagues have carried out an investigation into the association of anginal pain with mitral stenosis. Beginning with 1000 patients they excluded the following groups: (a) all patients in whom the onset of angina occurred after the age of 50, (b) women who had undergone hysterectomy, (c) patients with concurrent evidence of aortic stenosis, (d) all patients with hypertension or a history of myocardial infarction, and (e) hypo- or hyper-thyroidism. Of the 732 remaining patients the authors concluded that in 28 (3.8%) the anginal symptoms were attributable exclusively to the effects of valvular disease. On the whole these patients were young (average age 34 years) and they seemed to be rather liable to attacks of left ventricular failure brought on directly by physical effort.

Electrocardiograms at rest and after exertion, together with the absence of coronary atherosclerosis at necropsy in this group, raise the interesting possibility that the underlying cause of anginal pain may be the impairment of coronary circulation due to increased resistance in the pulmonary arterioles combined with a diminished cardiac reserve. One of the major conclusions reached is that anginal pain in a patient with mitral stenosis whose aortic valve is healthy, and who has no history of coronary thrombosis, is an indication for valvotomy.

ITALY

Rheumatic heart disease in Milan schoolchildren.—In a review of the incidence of rheumatic heart disease among schoolchildren in Milan during the period, 1934-57, E. Bucciante and G. Granata note that the incidence of severe forms was relatively low whereas mild forms were common. The over-all mortality rate was 8.5% and was particularly high among those with severe valvular involvement. The incidence of 'invalidism' was 22% among those with rheumatic fever and 7% among those with pararheumatic infections. Attention is drawn to the relatively low incidence of episodes of heart failure among these children with rheumatic heart disease, indicating that the child's heart is tolerant of valvular disturbances.

These are considered satisfactory findings and they are attributed to the small number of relapses which in turn is considered to be due to the careful prophylactic measures which have been maintained at the city's cardiological centre since its inception. In the earlier years these included the periodical administration of salicylates, and tonsillectomy when indicated. Latterly they have included the administration of antibiotics and steroids.

Tuberculosis immunization.—The Institut Toscan has recently published evidence gathered during the past ten years concerning the effectiveness, in guinea-pigs, of protective immunization using a special formalized vaccine developed by Petragnani and known as A.I.P. (Anatubercoline Integrale de Petragnani). It is evident that the immunity resulting from the use of this substance is 'at least equal' to that obtained from B.C.G. vaccine when both are administered by the multiple puncture technique.

Among the other conclusions to emerge from this study are the following: (1) Mantoux conversion follows more swiftly, and endures longer, after immunization with B.C.G. than with A.I.P. (2) Administration of minimal doses of killed *M. tuberculosis* caused the rapid reappearance of tuberculin allergy in those animals in which it had disappeared. (3) The immunizing power of A.I.P. appears to be unrelated to its ability to provoke sensitivity to tuberculin, whereas it is closely associated with the capacity to excite an allergic response to *M. tuberculosis* itself. (4) Repeated small doses are more effective than a single large dose in bringing about a state of specific immunity.

The report not only refers to the results gathered from observations made on 12,000 human vaccinations, and to the confirmation thus afforded of the experimental work on which they were based, but draws attention to the fact that the incidence of tuberculosis was more than twice as great in those who had not been vaccinated as among patients protected by this method.

Electrocardiographic changes in virus infections.—In an investigation of patients with infective hepatitis, encephalitis, virus pneumonia and influenza, L. Salonna and his colleagues draw attention to certain electrocardiographic changes which, they suggest, may be due to neurovascular instability or metabolic disturbances. The alterations most commonly observed were to be found in the ST complex or the T wave itself but there appeared to be no correlation with any clinical evidence of damage to the heart. Indeed, in many cases this was the only evidence of cardiac involvement and it is concluded that this transient manifestation is hardly ever the result of structural changes due to the underlying inflammatory process. In all the patients studied it appears that, whereas the electrocardiographic abnormalities were among the early manifestations of the disease their resolution was gradual and ran parallel with progress towards clinical recovery.

'Notes from the Continent' are produced in collaboration with the Editors of ***Bruxelles-Médical*** (Belgium), ***Le Concours Médical*** (France), ***Münchener Medizinische Wochenschrift*** (Germany), and ***Minerva Medica*** (Italy).

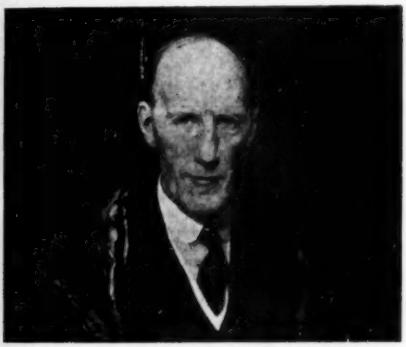
THE PRACTITIONER

Fifty Years Ago

AUGUST 1911

'Tetchy and wayward was thy infancy'.
Shakespeare: *King Richard III*, *IV*, iv, 168.

'No organ is more subject to nervous influences than the heart', writes Samuel West, M.D., F.R.C.P., Physician and Lecturer on Medicine at St. Bartholomew's Hospital, in 'Heart strain, with some remarks on training and other allied cardiac conditions'. Discussing the Nauheim treatment, the essential principle of which is gradual exercise under supervision, he com-



Sir Robert Hutchison, Bt, M.D., F.R.C.P.
(1871-1960)

ments 'there is nothing specially new in this . . . All that Nauheim can do, short of change of scene and life, can be equally well done at home'.

Robert Hutchison, M.D., F.R.C.P., Physician to the London Hospital, begins his article on 'Cœliac disease' by referring to the condition's curious history. 'It was first described by Gee in the year 1888', but 'even now it is by no means generally recognized, nor has a description of it found its way into the text-books'. He comments on the unusual precocity commonly present 'along with a tendency for the child to be unduly interested in his own symptoms, which is most unusual at this age. Sometimes, indeed, they are actual little hypochondriacs, and almost always they are spoilt'.

Born at Kirkliston, Midlothian, Robert Hutchison graduated with first class honours at Edinburgh University in 1893. After postgraduate work in Paris and Strasbourg and house posts in Edinburgh, he was appointed house physician at The Hospital for Sick Children, Great Ormond Street, in 1896, the year in which he obtained his M.D. and the M.R.C.P. Edinburgh. In 1897 he became M.R.C.P. London, and began to assist Dr. (later Sir Leonard) Hill in the physiology department of the London Hospital. He served both hospitals as assistant physician, physician, and consulting physician, and in an age when diagnostic 'aids' and 'wonder' drugs were less in evidence than today generations of students were taught the art of clinical examination without fuss and treatment without frills. A wider public benefited through his mastery of the spoken and the written word, for his name is associated with some fourteen books, including the celebrated 'Index of Treatment', 'Food and the Principles of Dietetics', 'Clinical Methods' ('the bible of the Membership examination'), and the delightful 'Lectures on Diseases of Children'.

Hutchison was active in the formation of the Association of Physicians, and served on the original editorial board of the *Quarterly Journal of Medicine*. Elected F.R.C.P. London in 1903, he was Goulstonian lecturer in 1904, Harveian orator in 1931, President of the Royal College of Physicians in 1938, and President of the Royal Society of Medicine in 1934. He gave much time to the affairs of the British Medical Association, and attended many of the overseas meetings. A baronetcy was conferred on him in 1939. Many have described his tall figure, dignified manner, austere expression, and hatred of humbug, the invective and alliteration when the 'curious collection of crapulous cretins creeping from crib to crib' earned his admonishment, and which ensured that his juniors learned from their mistakes. Hutchison's death at his home at Streatley in Berkshire at the age of 88 saw the passing of a great clinician—one who had heeded his own warning that 'It is always well, before handing the cup of knowledge to the young, to wait until the froth has settled'.

In his article on 'Abdomino-pelvic pain in women without physical signs of disease', Victor Bonney, M.D., M.S., M.R.C.P., F.R.C.S., Assistant Gynæcologist to the

Middlesex Hospital; Senior Surgeon to Out-patients, Chelsea Hospital for Women, says: 'In general I think it will be agreed that women exhibit greater fortitude towards those varieties of pain that afflict either sex than do men'. He goes on to say, however, that the 'transient and protean characters' of abdomino-pelvic pains make elucidation difficult, whilst 'the tendency to illogical exaggeration naturally pertaining to the sex is unduly developed in these women, and leads to the use of language when describing their symptoms widely out of proportion to the actual facts'. Condemning removal of a normal ovary for so-called 'ovarian' pain, he adds: 'Still worse is it to remove normal ovaries on both sides, a practice now happily obsolete. Patients of the class with which this paper deals are particularly ill suited to bear the nervous symptoms that result from a premature and artificial menopause'.

W. Blair Bell, M.D., Assistant Gynæcological Surgeon, Royal Infirmary, Liverpool, begins his contribution on 'Puerperal septic thrombo-phlebitis of the pelvic veins', by pointing out that 'it is only in recent years' that the condition 'has come to be looked upon as a pathological lesion amenable to surgical treatment . . . I am fully persuaded that when every case of septic thrombo-phlebitis of the pelvic veins is operated upon in the early stages the mortality will drop to, say, 5 per cent. as against the 60 per cent. of those treated by expectant methods'.

'Intussusception', discussed by Albert J. Walton, M.S., F.R.C.S., Assistant Surgeon, Greenwich Hospital; Senior Registrar, London Hospital, is described as 'one of the commonest causes of intestinal obstruction'. The prognosis 'will depend very largely upon the length of time the lesion has existed . . . at the Glasgow Royal Infirmary, out of 123 cases, of those with only 6-24 hours' history, 61 per cent. recovered'.

'A portable metal operating table', 'sold at the moderate price of £10 10s. complete', is the main item in 'Preparations, Inventions, etc.' this month. Weighing 'under 50 lbs. and folding up into a space of 32 in. x 20 in. x 6 in., it is opened and fixed ready for use in 30 seconds'. Made to the requirements of Mr. Bernard J. Ward, F.R.C.S., it is claimed to mark 'an advance in the construction of operating tables with ease of erection'.

T. H. B.

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in the diabetic diet

Clinical references to the diabetic syndrome can be traced to ancient Egyptian writings, and various forms of dietary treatment have been practised for centuries. The discovery of insulin in 1921 completely changed the outlook in diabetes, but adherence to a low-carbohydrate diet still remains an essential part of the treatment.

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